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XUM

889. *Formation and Properties of Sydnone Imines, a New Class of Meso-ionic Compound, and Some Sydnones Related to Natural α-Amino-acids.*

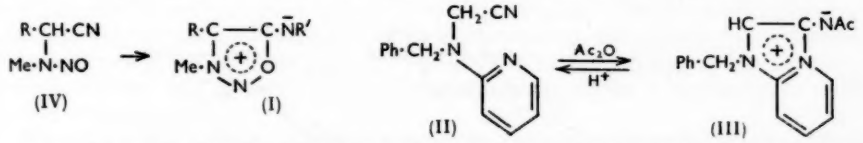
By Peter Brookes and James Walker.

When two representative α-methylamino-nitriles were treated with excess of nitrous fumes and the crude products were treated with acetic anhydride, sydnone nitroimines were formed by dehydration of the intermediate sydnone imine nitrates. Sydnone imine salts are formed with great ease from α-*N*-methyl-*N*-nitrosoamino-nitriles by reaction with an equivalent of nitric acid, or with hydrogen chloride in ether. The parent free sydnone imines were unstable and liberation from the salt gave the corresponding α-(*N*-methyl-*N*-nitrosoamino)-acid amide. Catalytic hydrogenation of 3-methyl-4-*iso*propyl-sydnone imine nitrate gave *N*-methylvaline amide and ammonia.

Besides their formation by dehydration with acetic anhydride, the sydnone nitroimines were also obtained by treatment of the nitrates with concentrated sulphuric acid. The nitroimines were stable to acid but decomposed immediately in presence of alkali with liberation of nitrous oxide and formation of the α-(*N*-methyl-*N*-nitrosoamino)-acid.

Several sydnones bearing side-chains characteristic of natural α-amino-acids have been prepared.

As a preliminary stage in the preparation of sydnones related to natural α-amino-acids, which is described below, α-methylamino*iso*valeronitrile and γ-methyl-α-methylamino-valeronitrile were prepared as intermediates in the preparation of *N*-methylvaline and *N*-methyl-leucine respectively. It therefore appeared of interest to nitrosate these two nitriles and to attempt the formation of the corresponding sydnone imines (I; R′ = H).



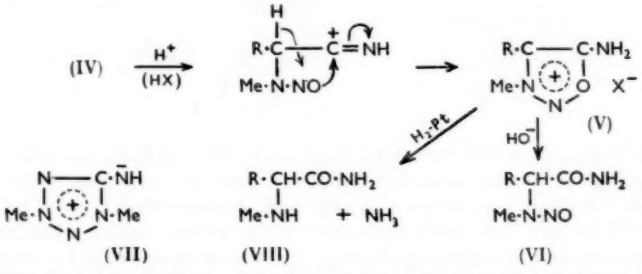
As a guide to the behaviour that might have been expected from this hitherto unknown type of compound * one may note that Bristow, Charlton, Peak, and Short [1] had shown that *N*-benzyl-*N*-2-pyridylamino-acetaldoxime and -acetonitrile (II) were both converted by acetic anhydride into " an acetyl derivative of the nitrile," which contained no cyano-group (from its infrared absorption spectrum) and was formulated as the meso-ionic compound (III). On cold acid hydrolysis the latter (III) was deacetylated and reverted to the nitrile (II). This behaviour of (III) suggested that it might not be possible to demonstrate the formation of the sydnone imine (I; R′ = H) unless steps were taken to stabilise the structure, as, for example, by acetylation to give the sydnone acetylimine (I; R′ = Ac), and the normal conditions used for sydnone formation from α-[*N*-alkyl(or aryl)-*N*-nitroso-amino]-acids, namely, the action of acetic anhydride, could be expected to lead to acetylated imines (I; R′ = Ac) when applied to α-(*N*-methyl-*N*-nitrosoamino)-nitriles (IV). Acetic anhydride, however, had no effect on pure α-(*N*-methyl-*N*-nitrosoamino)*iso*valeronitrile (IV; R = Pr^{i}), but treatment of α-methylamino*iso*valeronitrile with nitrous fumes in excess followed by treatment of the crude product with acetic anhydride at room temperature gave a crystalline solid $C_6H_{10}O_3N_4$, which appeared to contain no cyano-group from its infrared absorption spectrum and showed two strong bands in its ultraviolet

* Baker, Ollis, and Poole (*J.*, 1949, 311) had foreseen the possible existence of sydnone alkyl- or aryl-imines (I; R′ = alkyl or aryl), although none has so far been described.

[1] Bristow, Charlton, Peak, and Short, *J.*, 1954, 616.

XUM

absorption spectrum suggestive of an aromatic system. Similar treatment of γ-methyl-α-methylaminovaleronitrile afforded a homologous substance $C_7H_{12}O_3N_4$, having an almost identical ultraviolet absorption spectrum and showing many features in common with the preceding substance $C_6H_{10}O_3N_4$ in its infrared absorption spectrum. In a subsequent experiment the crude unwashed α-(*N*-methyl-*N*-nitrosoamino)*iso*valeronitrile, when left overnight, partly solidified and the solid after purification gave analytical figures indicative of the formula $C_6H_{12}O_4N_4$; the ultraviolet absorption spectrum of this substance showed a single maximum at 300 mμ and the infrared absorption spectrum showed a strong band at 1670 cm.$^{-1}$, with a subsidiary band at 1615 cm.$^{-1}$. Similar treatment of γ-methyl-α-methylaminovaleronitrile gave a substance $C_7H_{14}O_4N_4$ with closely similar light-absorption properties to those of the substance $C_6H_{12}O_4N_4$. As the substance $C_6H_{12}O_4N_4$ was a nitrate it was obviously derived from a base $C_6H_{11}ON_3$, and the similarity between the ultraviolet light absorption and that of 3-*cyclo*hexyl-[2] and 3-benzyl-sydnone [2,3] suggested that the substance $C_6H_{12}O_4N_4$ was, in fact, 3-methyl-4-*iso*propylsydnone imine nitrate (V; R = Pr^i, X = NO_3). It was then found to be more conveniently accessible by treating pure α-(*N*-methyl-*N*-nitrosoamino)*iso*valeronitrile (IV; R = Pr^i) with an equivalent amount of nitric acid, and the hydrochloride (V; R = Pr^i, X = Cl) was obtained by the action of hydrogen chloride in dry ether * on the methylnitrosoamino-nitrile (IV; R = Pr^i). Similarly the substance $C_7H_{14}O_4N_4$ was shown to be 4-*iso*butyl-3-methylsydnone imine nitrate (V; R = Bu^i, X = NO_3) by its ready formation from pure γ-methyl-α-(*N*-methyl-*N*-nitrosoamino)valeronitrile (IV; R = Bu^i) and nitric acid, and the hydrochloride (V; R = Bu^i, X = Cl) resulted from the action of dry hydrogen chloride in ether. The nitrate (V; R = Pr^i, X = NO_3) was converted into the hydrochloride (V; R = Pr^i, X = Cl) by treatment with the chloride form of an anion-exchange resin, but treatment with the hydroxyl form of the resin opened the heterocyclic ring and gave the α-(*N*-methyl-*N*-nitrosoamino)-acid amide (VI; R = Pr^i), which was also obtained when the neutral aqueous solution of the nitrate (V; R = Pr^i, X = NO_3) was basified in the



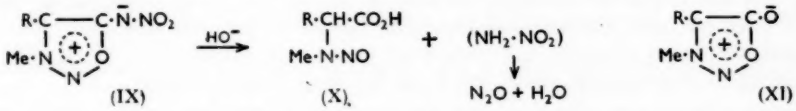
cold and extracted with chloroform. It thus appears that the sydnone imine (I; R = Pr^i, R′ = H) is incapable of existence as the free base in contrast, for example, with 5-imino-1 : 3-dimethyltetrazole (VII), a meso-ionic imine, which can be handled as the free base.[4] The conversion of the sydnone imine nitrate (V; R = Pr^i, X = NO_3) into the α-(*N*-methyl-*N*-nitrosoamino)-amide (VI; R = Pr^i) on treatment with alkali is formally analogous to the reversion,[5] under rather more vigorous alkaline conditions, of sydnones to their parent α-[*N*-alkyl(or aryl)-*N*-nitrosoamino]-acids. Also, as in the catalytic hydrogenation

* *Added, July 6th*, 1957.—Reference was made to the present work recently by Baker and Ollis (*Quart. Rev.*, 1957, **11**, 15), and, as a result, Professor M. Ohta (Tokyo) has written to say that he and his colleagues have obtained sydnone imine hydrochlorides by the action of ethanolic hydrogen chloride on suitably substituted nitriles (Kato, Hashimoto, and Ohta, *J. Chem. Soc. Japan*, 1957, **78**, 707).

[2] Baker, Ollis, and Poole, *J.*, 1949, 311.
[3] Earl, Le Fèvre, and Wilson, *ibid.*, p. S 103.
[4] Bryden, Henry, Finnegan, Boschan, McEwan, and Van Dolah, *J. Amer. Chem. Soc.*, 1953, **75**, 4863; Henry, Finnegan, and Lieber, *ibid.*, 1954, **76**, 2894.
[5] Earl and Mackney, *J.*, 1935, 899.

of sydnones [2] to the α-*N*-alkyl(or aryl)amino-acid and ammonia, 3-methyl-4-*iso*propylsydnone imine nitrate (V; R = Pr^i, X = NO_3) took up two mols. of hydrogen rapidly and a third more slowly with formation of *N*-methylvaline amide (VIII; R = Pr^i) and ammonia.

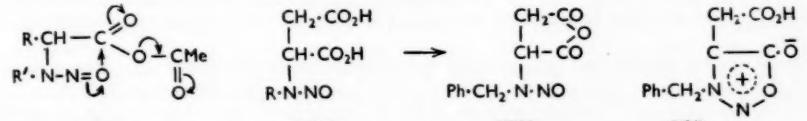
Returning to the compounds $C_6H_{10}O_3N_4$ and $C_7H_{12}O_3N_4$, it is obvious, in view of the ready formation of the sydnone imine nitrates (V; R = Pr^i, Bu^i, X = NO_3) from the α-(*N*-methyl-*N*-nitrosoamino)-nitriles (IV; R = Pr^i, Bu^i), that they were formed in the circumstances outlined above by dehydration of sydnone imine nitrates by the action of acetic anhydride analogously to the dehydration of aryl- [6] and alkyl-amine nitrates [7] by acetic anhydride to give aryl- or alkyl-nitramines. The same substances $C_6H_{10}O_3N_4$ and $C_7H_{12}O_3N_4$ were also obtained by the action of cold concentrated sulphuric acid on the sydnone imine nitrates (V; R = Pr^i or Bu^i, X = NO_3), similarly to the conversion of urea nitrate into nitrourea.[8] The substances $C_6H_{10}O_3N_4$ and $C_7H_{12}O_3N_4$ are therefore formulated as the meso-ionic 3-methyl-4-*iso*propylsydnone nitroimine (IX; R = Pr^i) and 4-*iso*butyl-3-methylsydnone nitroimine (IX; R = Bu^i) respectively. These substances were stable towards cold mineral acid and water but they were immediately decomposed by aqueous alkali, the products in the case of 3-methyl-4-*iso*propylsydnone nitroimine (IX; R = Pr^i) being identified as *N*-methyl-*N*-nitrosovaline and nitrous oxide. The latter product, identified by its infrared absorption spectrum, is presumably formed by way of nitramide.



(IX) (X) (XI)

No biological properties of sydnones appear to have been recorded, and, as it appeared probable that suitably substituted sydnones might act as amino-acid antagonists, a number of sydnones (XI) were prepared from *N*-methylamino-acids. The *N*-methylamino-acids employed were sarcosine, *N*-methylvaline, *N*-methyl-leucine, and *N*-methylphenylalanine. *N*-Methyl-leucine was prepared from *iso*valeraldehyde by the method used in the case of *N*-methylvaline,[9] and *N*-methylphenylalanine was prepared by a simplification of the method of Knoop and Oesterlin.[10]

Nitrosation was best carried out in aqueous solution with nitrous fumes, and sydnone formation from the *N*-methyl-*N*-nitrosoamino-acids was effected with acetic anhydride. 3-Methylsydnone (XI; R = H) and 4-*iso*butyl-3-methylsydnone (XI; R = Bu^i) could



(XII) (XIII) (XIV) (XV)

not be obtained solid at room temperature and distillation in a vacuum was accompanied by slight decomposition, but 3-methyl-4-*iso*propyl- (XI; R = Pr^i) and 4-benzyl-3-methylsydnone (XI; R = CH_2Ph) were obtained crystalline. The ultraviolet spectra of these four compounds were very similar; the 4-substituted compounds (XI; R = Pr^i, Bu^i, CH_2Ph) showed a single strong band at 292 mμ (log ε 3·89—3·98) in agreement with Baker, Ollis, and Poole,[2] who regard absorption at 292 mμ as characteristic of the sydnone ring, while in 3-methylsydnone (XI; R = H) the maximum was shifted to 286 mμ. The

[6] Bamberger, *Ber.*, 1895, **28**, 399; Hoff, *Annalen*, 1900, **311**, 99.
[7] Bamberger, *Ber.*, 1895, **28**, 535.
[8] Lachman and Thiele, *Ber.*, 1894, **27**, 1519.
[9] Cook and Cox, *J.*, 1949, 2334.
[10] Knoop and Oesterlin, *Z. physiol. Chem.*, 1925, **148**, 310.

infrared spectra showed multiple bands [11] in the 1650—1800 cm.$^{-1}$ region, the numbers, positions, and relative intensities of the maxima depending markedly on the media in which the spectra were observed (homogeneous film, $CHCl_3$, CCl_4, EtOH, or KCl disc).

Baker, Ollis, and Poole [12] have provided evidence to show that sydnone formation with acetic anhydride takes place by way of a mixed anhydride (XII), and that conversion of the latter into the sydnone occurs relatively slowly by attack by the anionoid nitroso-oxygen atom on the proximate cationoid carbonyl group. Particular interest therefore attached to the behaviour of an *N*-alkyl-*N*-nitrosoaspartic acid (XIII) under the conditions of sydnone formation with acetic anhydride. *N*-Methylaspartic acid, readily obtained by addition of methylamine to maleic acid, gave, however, an oily nitroso-derivative, and *N*-benzylaspartic acid was therefore used instead, as it gave a solid nitroso-derivative (XIII; R = CH_2Ph). Treatment of the latter with acetic anhydride gave a crystalline anhydro-compound $C_{11}H_{10}O_4N_2$, showing a single rather broad band in its ultraviolet absorption spectrum at 242 mμ and two strong typical carbonyl-stretching bands in its infrared absorption spectrum at 1785 and 1865 cm.$^{-1}$, indicative of the cyclic anhydride * structure (XIV), together with a band at 1400 cm.$^{-1}$ probably due to the >N·NO group.[11a] Obviously steric and polar constraints inhibiting approach of the nitroso-oxygen atom to the carbonyl-carbon atom prevent isomerisation of *N*-benzyl-*N*-nitrosoaspartic anhydride (XIV) to 3-benzyl-4-carboxymethylsydnone (XV).

The *N*-methylamino-acids and the four sydnones were kindly examined by Dr. A. T. Fuller and Mr. J. Lee for inhibitory activity *in vitro* against *Strep. haemolyticus*, *Staph. aureus*, *Bact. coli*, and *Leuconostoc mesenteroides* but no activity was observed. The four sydnones, the sydnone imines, and nitroimines were kindly examined by Dr. R. J. Terry for activity in experimental filarial infections but none showed activity.

Experimental

3-Methyl-4-isopropylsydnone Imine Nitrate (V; R = Pr^i; X = NO_3).—(*a*) 2-Methylamino-*iso*valeronitrile [9] (11·2 g.) was dissolved in dry ether (50 c.c.), the solution was cooled in ice, and nitrous fumes, generated by the action of 25% sulphuric acid on solid sodium nitrite, were passed until the solution became deep blue-green in colour (1½—2 hr.). The solvent was removed at room temperature, giving a pale brown liquid (16·5 g.), which evolved nitrous fumes on warming. The liquid did not crystallise and the ultraviolet light absorption spectrum showed only end-absorption. When kept at room temperature for 3 days the liquid deposited crystals. Ether was added and the pale yellow solid (6·5 g.) was collected and crystallised from ethanol–ether, giving colourless needles of *3-methyl-4-isopropylsydnone imine nitrate*, m. p. 135—136° (Found: C, 35·5; H, 6·0; N, 26·8. $C_6H_{11}ON_3,HNO_3$ requires C, 35·3; H, 5·9; N, 27·4%). Low nitrogen figures were regularly obtained with substances containing the NNO structure.

Nitrate ion was determined qualitatively and quantitatively as follows: (i) aqueous solutions of the above substance (0·2 g.) and *p*-acetylphenylguanidine hydrochloride [13] (0·21 g.) were mixed. *p*-Acetylphenylguanidine nitrate (0·24 g.) separated immediately and crystallised from water in colourless prisms, m. p. 242°, in agreement with King and Tonkin,[13] not depressed on admixture with an authentic specimen. (ii) A solution of the substance (217·7 mg.) in water (10 c.c.) and acetic acid (1 c.c.) was heated nearly to boiling and treated with a 10% solution of nitron in acetic acid (10 c.c.). The solution was cooled in ice for 1 hr. before collection of the precipitated nitron nitrate (410 mg.) in a tared crucible (Found: NO_3^-, 31·1. $C_6H_{11}ON_3,HNO_3$ requires NO_3^-, 30·4%).

(*b*) α-(*N*-Methyl-*N*-nitrosoamino)*iso*valeronitrile (2·8 g.) (see below) was mixed with 95% nitric acid (1·4 g.), and the mixture was kept at room temperature for 18 hr.; it set to a mass of

* Cf. succinic anhydride, $\nu_{max.}$ 1782 and 1865 cm.$^{-1}$ (Bellamy, "The Infrared Spectra of Complex Molecules," Methuen, London, 1954, p. 111).

[11] Cf. (*a*) Earl, Le Fèvre, Pulford, and Walsh, *J.*, 1951, 2207; (*b*) Fugger, Tien, and Hunsberger, *J. Amer. Chem. Soc.*, 1955, **77**, 1843.

[12] Baker, Ollis, and Poole, *J.*, 1950, 1542.

[13] King and Tonkin, *J.*, 1946, 1063.

crystals. Recrystallisation from ethanol–ether gave colourless needles (3·56 g.) of 3-methyl-4-*iso*propylsydnone imine nitrate, m. p. 136°, identical (infrared absorption spectrum) with the substance prepared as in (*a*) (above). The ultraviolet absorption spectrum showed a single maximum at 300 mμ (log ε 3·97).

3-Methyl-4-isopropylsydnone Imine Hydrochloride (V; R = Pr^{i}, X = Cl).—(*a*) The above nitrate (0·2 g.), dissolved in water (10 c.c.), was passed slowly through a column (10 cm. × 0·5 cm.) of " Amberlite IRA-400 " in the chloride form. The effluent from the column remained neutral throughout and evaporation afforded the *hydrochloride* (0·17 g.), which separated from ethanol–ether in colourless needles, m. p. 185° (Found: C, 40·7; H, 6·4; Cl, 20·1. $C_6H_{11}ON_3$,HCl requires C, 40·6; H, 6·8; Cl, 20·0%). (*b*) α-(*N*-Methyl-*N*-nitrosoamino)*iso*valeronitrile (2·0 g.) was dissolved in dry ether (10 c.c.) and the solution was saturated with dry hydrogen chloride. White crystals (2·2 g.) separated immediately and recrystallisation from ethanol–ether gave the sydnone imine hydrochloride, m. p. 185°, identical with the substance prepared as in (*a*) (above).

4-isoButyl-3-methylsydnone Imine Nitrate (V; R = Bu^{i}, X = NO_3).—(*a*) γ-Methyl-α-methylaminovaleronitrile (2·0 g.) was treated with nitrous fumes in the manner described above in the case of the lower homologue (*a*) (above). Recrystallisation of the product from ethanol–ether afforded colourless prisms (1·5 g.) of *4-isobutyl-3-methylsydnone imine nitrate*, m. p. 91—93° (Found: C, 38·8; H, 6·5. $C_7H_{13}ON_3$,HNO_3 requires C, 38·5; H, 6·4%). The ultraviolet absorption spectrum showed a single maximum at 300 mμ (log ε 3·96).

(*b*) γ-Methyl-α-(*N*-methyl-*N*-nitrosoamino)valeronitrile (1·55 g.) was mixed with 95% nitric acid (0·67 g.) and kept at room temperature for 18 hr. The mixture solidified when scratched. Recrystallisation of the resulting solid from ethanol–ether afforded prisms (1·8 g.) of the nitrate, m. p. 91—93°, identical (infrared absorption spectrum) with the substance prepared as in (*a*) (above).

4-isoButyl-3-methylsydnone Imine Hydrochloride (V; R = Bu^{i}, X = Cl).—A solution of γ-methyl-α-(*N*-methyl-*N*-nitrosoamino)valeronitrile (1·5 g.) in dry ether (5 c.c.) was saturated with dry hydrogen chloride. The precipitated *hydrochloride* (1·65 g.) separated from methanol–ethyl acetate in colourless needles, m. p. 165° (Found: C, 43·8; H, 7·2. $C_7H_{13}ON_3$,HCl requires C, 43·9; H, 7·3%). The ultraviolet absorption spectrum showed a single maximum at 300 mμ (log ε 3·96).

α-(N-Methyl-N-nitrosoamino)isovaleronitrile (IV; R = Pr^{i}).—α-Methylamino*iso*valeronitrile [9] (11·2 g.) was dissolved in dry ether, and nitrous fumes were passed in until the solution became pale green (*ca.* 1 hr.). The solution was washed with water, dried, and fractionated, affording *α-(N-methyl-N-nitrosoamino)isovaleronitrile* as a pale yellow oil (11·0 g.), b. p. 57—58°/0·3 mm., n_D^{21} 1·4580 (Found: C, 51·2; H, 7·7; N, 29·4. $C_6H_{11}ON_3$ requires C, 51·1; H, 7·8; N, 29·8%).

The substance was recovered unchanged (b. p., n_D) after treatment in the cold for 6 days with 3 parts of acetic anhydride and after 4 hr. on the steam-bath with 4 parts of acetic anhydride.

γ-Methyl-α-(N-methyl-N-nitrosoamino)valeronitrile (IV; R = Bu^{i}).—(i) *iso*Valeraldehyde (43 g.) was added with stirring to a solution of sodium metabisulphite (48 g.) in water (125 c.c.), the mixture being cooled in melting ice. After 30 min. 33% w/v aqueous methylamine (70 c.c.) was added, followed, after a further 30 min., by finely powdered potassium cyanide (33 g.). Stirring was continued for 1 hr., an oil separating. Extraction with ether and fractionation of the dried extract gave γ-methyl-α-methylaminovaleronitrile as a pale yellow oil (40 g.), b. p. 82—85°/15 mm., n_D^{21} 1·4351.

(ii) The preceding nitrile (6·0 g.) was treated with nitrous fumes in the manner described for the lower homologue (above), affording *γ-methyl-α-(N-methyl-N-nitrosoamino)valeronitrile* as a pale yellow oil (6·2 g.), b. p. 74°/0·4 mm., n_D^{21} 1·4594 (Found: C, 54·3; H, 8·5. $C_7H_{13}ON_3$ requires C, 54·3; H, 8·4%).

Attempted Preparation of 3-Methyl-4-isopropylsydnone Imine Free Base.—(*a*) 3-Methyl-4-*iso*propylsydnone imine nitrate (0·25 g.) was dissolved in water (10 c.c.) and applied to a column of " Amberlite IRA-400 " in the hydroxyl form. The effluent from the column was neutral throughout and evaporation gave a white solid (0·2 g.), affording on crystallisation from chloroform–light petroleum colourless needles of *α-(N-methyl-N-nitrosoamino)isovaleramide*, m. p. and mixed m. p. 159—161° (Found: C, 45·4; H, 8·0. $C_6H_{13}O_2N_3$ requires C, 45·3; H, 8·2%); an authentic specimen, obtained by esterification of *N*-methyl-*N*-nitrosovaline (see below) with diazomethane and shaking the resulting ester with concentrated aqueous ammonia for 24 hr.,

had m. p. 158—161° after recrystallisation from chloroform–light petroleum (Found: C, 45·3; H, 7·9%). (*b*) A solution of the nitrate (1·0 g.) in water (10 c.c.) was basified by the addition of 40% aqueous sodium hydroxide (0·5 c.c.). The solution was extracted with ether (3 × 10 c.c.) and evaporation of the dried extract gave α-(*N*-methyl-*N*-nitrosoamino)*iso*valeramide (0·7 g.), m. p. 159—161° after recrystallisation from chloroform–light petroleum (Found: C, 45·7; H, 8·1%).

Catalytic Hydrogenation of 3-*Methyl*-4-iso*propylsydnone Imine Nitrate.*—The nitrate (0·28 g.) in methanol (10 c.c.) was shaken with hydrogen at room temperature and atmospheric pressure in presence of previously reduced Adams catalyst (50 mg.). Uptake of hydrogen proceeded rapidly during the first 15 min. (Found: 75 c.c. Calc. for $2H_2$: 67 c.c.), and continued for a further hour [Found (total): 96 c.c. Calc. for $3H_2$: 100 c.c.]. The catalyst was removed and the odour of ammonia was apparent during evaporation of the solvent. Crystallisation of the residue (0·17 g.) from methanol–ether afforded colourless needles of *N-methylvaline amide nitrate*, m. p. 169—172° (Found: C, 37·4; H, 7·6; N, 21·2. $C_6H_{14}ON_2,HNO_3$ requires C, 37·3; H, 7·8; N, 21·7%). An aqueous solution (193 mg. in 2 c.c.) was basified with 40% aqueous sodium hydroxide (0·3 c.c.) and extracted with chloroform (3 × 5 c.c.). The residue (90 mg.) obtained on evaporation of the dried chloroform extract crystallised from ether–light petroleum in colourless prisms, m. p. 90° (Found: C, 55·2; H, 10·8; N, 21·2. Calc. for $C_6H_{14}ON_2$: C, 55·4; H, 10·7; N, 21·6%), identical with an authentic specimen of *N*-methylvaline amide, prepared as described by Cook and Cox.[9]

The ammonia produced during the catalytic hydrogenation was estimated in a separate experiment. 3-Methyl-4-*iso*propylsydnone imine nitrate (49·2 mg.) was hydrogenated as above. The catalyst was removed and the filtrate was made alkaline with aqueous sodium hydroxide. The solvent and ammonia were distilled into 0·1N-hydrochloric acid (10 c.c.), and excess of acid was back-titrated (Found: 2·4 c.c. Calc. for $1NH_3$ per $C_6H_{11}ON_3,HNO_3$: 2·4 c.c.).

3-*Methyl*-4-iso*propylsydnone Nitroimine* (IX; R = Pr^i).–(*a*) α-Methylamino*iso*valeronitrile (11·2 g.) was nitrosated in dry ether in the usual way and the solvent was removed at room temperature without prior washing. The residual crude brown oil was treated with ice-cold acetic anhydride (40 g.), and the mixture was kept at room temperature for several days. The solution was then poured on crushed ice (100 g.), neutralised with ammonia, and extracted with chloroform. Evaporation of the dried extract gave an oil (2·4 g.), which crystallised when cooled and scratched. Recrystallisation from chloroform–light petroleum afforded 3-*methyl*-4-iso*propylsydnone nitroimine* as colourless needles, m. p. 147—148° (Found: C, 38·8; H, 5·4; N, 29·5. $C_6H_{10}O_3N_4$ requires C, 38·7; H, 5·4; N, 30·1%).

(*b*) 3-Methyl-4-*iso*propylsydnone imine nitrate (2·04 g.) was added in small portions to concentrated sulphuric acid (10 c.c.) cooled in ice. When all the solid had been added the solution was kept at room temperature for 30 min. before being poured on crushed ice (50 g.). The precipitate was collected, and the filtrate was extracted with chloroform, yielding a further quantity of the same product. On crystallisation from ethanol the combined product (1·55 g.) afforded colourless needles, m. p. 146—148°, identical with the product obtained in (*a*) (above). The ultraviolet light absorption spectrum showed maxima at 270 and 345 mμ with log ε 3·89 and 4·26 respectively.

4-iso*Butyl*-3-*methylsydnone Nitroimine* (IX; R = Bu^i).—(*a*) Nitrosation of γ-methyl-α-methylaminovaleronitrile followed by treatment with acetic anhydride was carried out as described above for the preparation (*a*) of the lower homologue. 4-iso*Butyl*-3-*methylsydnone nitroimine* separated from chloroform–light petroleum in pale yellow plates, m. p. 127—128° (Found: C, 42·4; H, 5·9. $C_7H_{12}O_3N_4$ requires C, 42·0; H, 6·0%). The ultraviolet light absorption spectrum showed maxima at 270 and 345 mμ with log ε 3·82 and 4·16 respectively.

(*b*) 4-*iso*Butyl-3-methylsydnone imine nitrate (0·55 g.) was added to concentrated sulphuric acid (3 c.c.) as described above for the preparation (*b*) of the lower homologue. Crystallisation of the product from chloroform–light petroleum afforded 4-*iso*butyl-3-methylsydnone nitroimine, m. p. 127—128°, identical with the substance obtained in (*a*) (above) (Found: C, 41·7; H, 6·0%).

Action of Alkali on 3-*Methyl*-4-iso*propylsydnone Nitroimine.*—The nitroimine (0·93 g.) was dissolved in hot water (20 c.c.) and treated dropwise with 40% aqueous sodium hydroxide (0·5 c.c.). Each addition of alkali caused the evolution of a colourless, odourless gas, which rekindled a glowing splint. When all the alkali had been added the solution was strongly acidified with concentrated hydrochloric acid and extracted with ether. The colourless oil

(0·65 g.) recovered from the dried extract failed to crystallise promptly; it was acidic, and the *S-benzylthiuronium salt* crystallised from aqueous ethanol in needles, m. p. 141—143° (Found: C, 51·6; H, 6·4; N, 17·5. $C_8H_{12}O_3N_2,C_8H_{10}N_2S$ requires C, 51·5; H, 6·7; N, 17·2%). This derivative was identical with an authentic specimen of the benzylthiuronium salt of *N*-methyl-*N*-nitrosovaline (see below).

The nitroimine (0·6 g.), dissolved in hot water (20 c.c.), was treated dropwise with 3N-sodium hydroxide (5 c.c.) while a slow stream of air was passed through the solution. The gas evolved was washed with 20% aqueous sodium hydroxide and concentrated sulphuric acid before being passed through a glass spiral immersed in liquid air. The inlet to the spiral was closed and the exit was connected to the previously evacuated gas cell of the infrared spectrophotometer. The liquid air was removed and the contents of the spiral were allowed to evaporate. The infrared spectrum of the gas, measured over the range 4000—1000 cm.$^{-1}$, was identical with that of nitrous oxide.

N-Methyl-leucine.—γ-Methyl-α-methylaminovaleronitrile (40 g.) was added slowly to ice-cold concentrated sulphuric acid (60 g.). The solution was heated at 100°, then cooled, and poured on crushed ice (50 g.). The resulting solution was refluxed for 24 hr., cooled, and neutralised with 50% aqueous sodium hydroxide. The precipitate was removed and the filtrate was taken to dryness. The combined solids were extracted with boiling methanol (4 × 500 c.c.). Concentration and cooling afforded *N*-methyl-leucine (24·5 g.), and further crude material (7 g.) on further concentration of the mother-liquors; the substance crystallised from methanol in colourless prisms which sublimed at 255—256° (Found: C, 57·8; H, 10·6; N, 9·8. Calc. for $C_7H_{15}O_2N$: C, 57·9; H, 10·3; N, 9·7%).

N-Methylphenylalanine.—Phenylpyruvic acid [14] (3·3 g.) was dissolved in 70% aqueous ethanol (30 c.c.), and 25% w/v aqueous methylamine (4·8 c.c.) was added. The mixture was shaken in hydrogen at 3 atm. and room temperature for 22 hr. in presence of 5% palladised charcoal (100 mg.). The solution was filtered and the residue was washed with alcohol, filtrate and washings yielding further crude crystalline product on evaporation. The catalyst was separated by solution of the combined solids in the minimum volume of boiling water and filtering. On cooling, *N*-methylphenylalanine separated in colourless plates (2·5 g.), m. p. (sublimes) 235—240° (Found: C, 67·2; H, 7·3; N, 7·7. Calc. for $C_{10}H_{13}O_2N$: C, 67·0; H, 7·3; N, 7·8%).

N-Methylaspartic Acid.—A mixture of maleic anhydride (9·8 g.) and water (25 c.c.) was boiled under reflux for 30 min., cooled in melting ice, and treated slowly with 25% w/v aqueous methylamine solution (25 c.c.). After 1 hr. at the b. p. the solution was concentrated to small bulk and then boiled with 25% aqueous sodium hydroxide (40 c.c.), methylamine being removed in a stream of air. The resulting solution was concentrated (to *ca.* 25 c.c.) and acidified with concentrated hydrochloric acid to pH 2. The precipitate (12·6 g.) obtained by the addition of an equal volume of ethanol was crystallised from aqueous ethanol, affording *N*-methyl-aspartic acid monohydrate as needles, m. p. 134°, which gave the anhydrous acid, m. p. 184°, at 100° in a vacuum (Found: C, 40·5; H, 6·1; N, 9·5. Calc. for $C_5H_9O_4N$: C, 40·8; H, 6·1; N, 9·5%).

N-Methylvaline was prepared by the method of Cook and Cox,[9] and *N*-benzylaspartic acid by that of Frankel, Liwschitz, and Amiel.[15]

Nitrosation.—The *N*-alkylamino-acids were dissolved in water with slight warming only, if necessary, and nitrous fumes, generated as described above, were passed to saturation. The crude products were recovered by extraction with ether and concentration of the dried extracts. *N*-Nitrososarcosine, *N*-methyl-*N*-nitrosoleucine, and *N*-methyl-*N*-nitrosoaspartic acid were obtained as brown oils. *N*-Methyl-*N*-nitrosovaline was obtained as a brown oil but the *S*-benzylthiuronium salt crystallised from aqueous ethanol in needles, m. p. 142—143° (Found: C, 51·2; H, 6·5. Calc. for $C_6H_{12}O_3N_2,C_8H_{10}N_2S$: C, 51·5; H, 6·7%).

N-Methyl-N-nitrosophenylalanine, obtained in 95% yield, crystallised from aqueous ethanol in colourless prisms, m. p. 148—150° (Found: C, 57·7; H, 5·8; N, 13·4. $C_{10}H_{12}O_3N_2$ requires C, 57·7; H, 5·8; N, 13·4%).

N-Benzyl-N-nitrosoaspartic acid (XIII; R = CH_2Ph), as first obtained, crystallised from ether–light petroleum in colourless needles of a *dihydrate*, which lost its solvent of crystallisation above 80° and then melted sharply at 146—147° (Found: C, 45·9; H, 5·7; N, 9·4; loss in a

[14] *Org. Synth.*, Coll. Vol. II, p. 519.
[15] Frankel, Liwschitz, and Amiel, *J. Amer. Chem. Soc.*, 1953, **75**, 331.

vacuum at 80°, 13·4. $C_{11}H_{12}O_5N_2,2H_2O$ requires C, 45·8; H, 5·6; N, 9·7; H_2O, 13·4%). The anhydrous *compound* separated on crystallisation of the dried material from ether–light petroleum as colourless needles, m. p. 146—147° (Found: C, 52·4; H, 4·6; N, 11·0. $C_{11}H_{12}O_5N_2$ requires C, 52·4; H, 4·8; N, 11·0%).

Sydnone Formation.—In each case the *N*-methyl-*N*-nitrosoamino-acid was dissolved in acetic anhydride and kept at room temperature for several days. The mixture was then poured into water and extracted with chloroform, the extracts being dried and evaporated to give the sydnone.

3-Methylsydnone (XI; R = H) obtained as an oil in 65% yield, crystallised at 0° in needles and melted again at room temperature. Recrystallisation from chloroform–light petroleum at a low temperature failed to raise the m. p. sufficiently to give a product solid at room temperature. The substance distilled at 140—142°/0·2 mm. (n_D^{25} 1·5163), with slight decomposition which is reflected in the analytical figures (Found: C, 37·5; H, 4·4. Calc. for $C_3H_4O_2N_2$: C, 36·0; H, 4·0%). Ultraviolet light absorption: $\lambda_{max.}$ 286 mμ (log ε 3·81). Hammick and Voaden [16] have mentioned this substance as having m. p. 36°, but no further details have been published.

3-*Methyl*-4-iso*propyl sydnone* (XI; R = Pr^i), obtained in 60% yield, separated from ether–light petroleum in colourless needles, m. p. 55—57° (Found: C, 50·6; H, 7·3; N, 19·4. $C_6H_{10}O_2N_2$ requires C, 50·7; H, 7·0; N, 19·7%). Ultraviolet light absorption: $\lambda_{max.}$ 296 mμ (log ε 3·93).

4-iso*Butyl*-3-*methylsydnone* (XI; R = Bu^i), obtained as an oil in 65% yield, crystallised at −5°; it distilled with slight decomposition at 120—121°/0·2 mm. and had n_D^{25} 1·5043 (Found: C, 52·8; H, 7·6. $C_7H_{12}O_2N_2$ requires C, 53·8; H, 7·7%). Ultraviolet light absorption: $\lambda_{max.}$ 292 mμ (log ε 3·89).

4-*Benzyl*-3-*methylsydnone* (XI; R = CH_2Ph), obtained in 80% yield, crystallised from water in colourless needles, m. p. 108—110° (Found: C, 63·0; H, 5·3; N, 14·4. $C_{10}H_{10}O_2N_2$ requires C, 63·2; H, 5·2; N, 14·7%). Ultraviolet light absorption: $\lambda_{max.}$ 292 mμ (log ε 3·96).

N-*Benzyl*-N-*nitrosoaspartic Anhydride* (XIV).—Anhydrous *N*-benzyl-*N*-nitrosoaspartic acid (7·5 g.) was dissolved in acetic anhydride (20 c.c.), and the mixture was kept at room temperature for 4 days, then shaken vigorously with ice-cold water (50 c.c.); a white solid (3·6 g.) separated. Extraction of the aqueous solution with chloroform gave a further crop (1·1 g.) of the same substance. Crystallisation from chloroform–light petroleum afforded N-*benzyl*-N-*nitrosoaspartic anhydride* as colourless plates, m. p. 136—138° (Found: C, 56·1; H, 4·2; N, 11·9. $C_{11}H_{10}O_4N_2$ requires C, 56·4; H, 4·3; N, 12·0%). Ultraviolet light absorption: $\lambda_{max.}$ 242 mμ (log ε 3·86).

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[*Received, May* 22*nd*, 1957.]

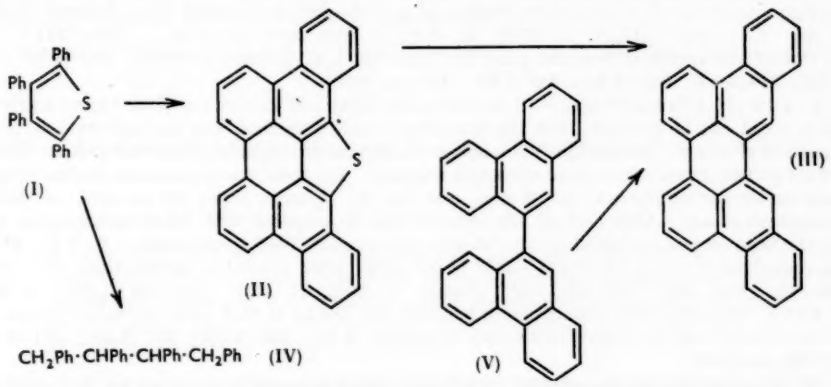
[16] Hammick and Voaden, *Chem. and Ind.*, 1956, 739.

890. *Synthetic Applications of Activated Metal Catalysts. Part V.* The Desulphurisation of Flavophen and of Tetraphenylthiophen.*

By G. M. Badger, B. J. Christie, Jenneth M. Pryke, and W. H. F. Sasse.

Desulphurisation of flavophen (II) with Raney nickel in boiling mesitylene yields 2 : 3-10 : 11-dibenzoperylene (III), identical with the product obtained from 9 : 9′-diphenanthryl with aluminium chloride. Desulphurisation of 2 : 3 : 4 : 5-tetraphenylthiophen gave 1 : 2 : 3 : 4-tetraphenylbutane and 1 : 2-diphenylethane.

The desulphurisation of organosulphur compounds with Raney nickel has been widely used for degradative work, but the applications of the method in organic syntheses have been recognised only recently. The desulphurisation of thiophencarboxylic acids, for example, has now been developed as a useful method for the synthesis of a variety of fatty acids.[1,2] It seemed likely that the reaction could also be applied in the preparation of aromatic hydrocarbons. The present paper reports the preparation of 2 : 3-10 : 11-dibenzoperylene (III) by the desulphurisation of flavophen (II), and the preparation of 1 : 2 : 3 : 4-tetraphenylbutane (IV) from 2 : 3 : 4 : 5-tetraphenylthiophen (I).



When 2 : 3 : 4 : 5-tetraphenylthiophen (I) is heated with aluminium chloride–sodium chloride it is cyclodehydrogenated to flavophen, for which structure (II) was suggested.[3] The sparing solubility of (II) precluded the use of the more usual solvents for the desulphurisation reaction, and a high-boiling solvent was therefore investigated. In pyridine some desulphurisation occurred, but 2 : 2′-dipyridyl was also obtained (this observation led to the development of a general method for the preparation of heterocyclic diaryls[4]). Some desulphurisation of flavophen was effected in xylene and in dimethylformamide but mesitylene was found to give the most satisfactory results. A further problem associated with the desulphurisation of flavophen was a tendency for the product to be partially hydrogenated, rendering final purification extremely difficult. This was avoided by the use of a Raney nickel catalyst containing less hydrogen than usual. A very high nickel : flavophen ratio was also required for complete desulphurisation, this

* Part IV, *J.*, 1957, 3862.

[1] Badger, Rodda, and Sasse, *J.*, 1954, 4162.

[2] Sy, Buu-Hoï, and Dat Xuong, *Compt. rend.*, 1954, **239**, 1224, 1813; 1955, **240**, 442, 785; *Bull. Soc. chim. France*, 1955, 1583; Sy, *ibid.*, p. 1175.

[3] Steinkopf, *Annalen*, 1935, **519**, 297.

[4] Badger and Sasse, *J.*, 1956, 616.

being much larger than with dibenzothiophen.[5] The high temperature of the reaction (leading to loss of loosely bound hydrogen) may be a factor here; but steric hindrance must also be of importance. The desulphurisation of flavophen was then found to yield 2 : 3-10 : 11-dibenzoperylene (III), identical with the material obtained by heating 9 : 9′-diphenanthryl (V) with aluminium chloride.[6] The desulphurisation therefore satisfactorily establishes the structure of flavophen.

2 : 3 : 4 : 5-Tetraphenylthiophen (I) was also more difficult to desulphurise than dibenzothiophen; but 1 : 2 : 3 : 4-tetraphenylbutane (IV) was obtained with either butanol or xylene as solvent. In the latter some 1 : 2-diphenylethane was obtained and only part of the starting material could be accounted for, suggesting that carbon–carbon hydrogenolysis is important in this case.

Experimental

Flavophen.—The following method was found to be better than that of Steinkopf.[3] Aluminium chloride (8 g.) and sodium chloride (2 g.) were heated at 130°. 2 : 3 : 4 : 5-Tetraphenylthiophen (2 g.; m. p. 182°) was added to the melt, which was maintained at 130°, with stirring by dry air, for 5 hr. After cooling, the mixture was decomposed with dilute hydrochloric acid, and washed with hot ethanol and benzene; the residue was sublimed at 300°/0·05 mm. and finally recrystallised from nitrobenzene or from ethyl benzoate. Flavophen (0·52 g.) was obtained as fine yellow needles, m. p. 378—380° (evacuated tube) (Found: C, 87·5; H, 3·7. Calc. for $C_{28}H_{14}S$: C, 87·9; H, 3·7%). Steinkopf [3] gives m. p. 391—392°. The ultraviolet absorption in benzene gave the following $\lambda_{max.}$ and log ε values: 280 (4·55); 296 (4·52); 310 (4·44); 324 (4·35); 385 (4·45); 410 mμ (4·49).

2 : 3-10 : 11-*Dibenzoperylene.*—(i) In our hands Zinke and Ziegler's method [6] gave a product which could not be purified; but the following modified method was satisfactory. 9 : 9′-Diphenanthryl (1·2 g.; Bachmann [7]) was added to aluminium chloride (4·8 g.) and sodium chloride (1·2 g.) at 140° in an atmosphere of carbon dioxide. The melt was maintained at this temperature under carbon dioxide for 9 min. (see ref. 6). Longer times led to tars, as did an atmosphere of air. After cooling, the mixture was decomposed with dilute hydrochloric acid, and the product was sublimed at 300°/25 mm. and recrystallised from xylene. 2 : 3-10 : 11-Dibenzoperylene (0·112 g.) had 334—336° (evac. tube) after several crystallisations (lit.,[6] m. p. 315—318°, 329—332°, and 343—345°) (Found: C, 95·2; H, 4·75. Calc. for $C_{28}H_{16}$: C, 95·4; H, 4·6%). Its ultraviolet absorption in benzene was similar to that given by Schauenstein and Burgermeister,[6] the $\lambda_{max.}$ and log ε values being 291 (4·44); 303 (4·56); 391 (4·18); 411 (4·46); and 439 mμ (4·50).

(ii) Desulphurisation was effected with Raney nickel prepared as described for W-7 catalyst [8] except that the digestion was carried out at 60—65°. Before use the catalyst was heated for ½ hr. at 100° and then washed repeatedly by decantation with methanol.

This Raney nickel (30 c.c.) was added through the condenser to flavophen (0·25 g.) in mesitylene (250 c.c.) at 100°. After the methanol had been distilled off, the mixture was refluxed for 5 hr., cooled to 100°, and filtered. The filtrate was concentrated to 50 c.c. *in vacuo*, and the product allowed to crystallise. 2 : 3-10 : 11-Dibenzoperylene (50 mg.) was obtained as light yellow-brown needles, m. p. 335—338° (evac. tube) not depressed by admixture with a specimen obtained as above. Its ultraviolet and infrared spectra were also identical with those given by the authentic material.

More of the product (35 mg.) was obtained by Soxhlet extraction of the catalyst with mesitylene and with xylene.

Desulphurisation of 2 : 3 : 4 : 5-*tetraphenylthiophen.*—(i) Desulphurisation could not be effected in methanol–benzene, but the following method was satisfactory. A mixture of tetraphenylthiophen (1 g.), W-7 Raney nickel [8] (15 c.c.), and butanol (100 c.c.) was refluxed for 5 hr. After separation of the nickel the solution was evaporated and the product dissolved in benzene.

[5] Badger and Sasse, *J.*, 1957, 3862.
[6] Zinke and Ziegler, *Ber.*, 1941, **74**, 115; Schauenstein and Bürgermeister, *Ber.*, 1943, **76**, 205; Ioffe, quoted by Clar, "Aromatische Kohlenwasserstoffe," Springer, 1952, p. 310.
[7] Bachmann, *J. Amer. Chem. Soc.*, 1934, **56**, 1363.
[8] Billica and Adkins, *Org. Synth.*, 1949, **29**, 24.

Addition of a little light petroleum precipitated some tetraphenylthiophen (0·1 g.). Chromatography of the resulting product, in light petroleum, and recrystallisation from light petroleum (b. p. 40—60°) gave 1 : 2 : 3 : 4-tetraphenylbutane (0·05 g.) as needles, m. p. 180° (Found: C, 93·05; H, 7·3. Calc. for $C_{28}H_{26}$: C, 92·8; H, 7·2%). Lit., m. p. 179—180°.

(ii) A mixture of tetraphenylthiophen (3 g.), W-7 Raney nickel (50 g., washed with methanol), and xylene (100 c.c.) was heated to remove water and methanol (3 hr.) and then refluxed for 7½ hr. The catalyst was washed with boiling xylene four times and the combined filtrates were evaporated. The product was chromatographed in light petroleum, followed by elution with light petroleum and finally with benzene. Evaporation of the first fractions gave a liquid which was twice distilled (0·07 g.; b. p. 67°/0·05 mm.), recrystallised from light petroleum (b. p. <40°), and sublimed (at 50°/0·01 mm.) to give prisms, m. p. 51·5° not depressed by admixture with an authentic specimen of 1 : 2-diphenylethane (Found: C, 92·4; H, 7·7. Calc. for $C_{14}H_{14}$: C, 92·3; H, 7·7%). Its infrared spectrum was also identical with that given by diphenylethane. The middle fractions of the chromatograph gave 1 : 2 : 3 : 4-tetraphenylbutane (0·9 g.) identical with the material described above; and the final fractions yielded traces of a fluorescent substance which could not be identified.

Dissolution of the catalyst with hydrochloric acid, followed by chromatography in light petroleum gave a brown oil (0·3 g.). Repeated chromatography in light petroleum yielded traces of 1 : 2-diphenylethane and a fluorescent substance which could not be identified.

We thank Dr. H. J. Rodda for the infrared spectra. Microanalyses were carried out by the C.S.I.R.O. Microanalytical Laboratory, Melbourne. We also express our thanks for an I.C.I.A.N.Z. Research Fellowship awarded to one of us (B. J. C.).

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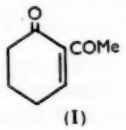
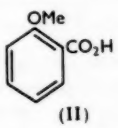
891. *Investigations on the Synthesis of 2-Acetylcyclohex-2-en-1-one. Part I.*

By (Miss) M. E. McENTEE and A. R. PINDER.

Reduction of *o*-anisic acid by sodium and ammonia yielded mainly 1 : 4-dihydro-*o*-anisic acid, but attempts to convert this into 2-acetyl*cyclo*hex-2-enone were unsuccessful. Chlorination and dehydrochlorination of 2-acetyl*cyclo*hexanone gave a liquid (probably 2-acetyl*cyclo*hex-3-en-1-one) and a crystalline product $C_{16}H_{20}O_4$.

THE possible use of 2-acetyl*cyclo*hex-2-en-1-one (I) as intermediate in steroid synthesis [1] has led to several attempts to synthesise it.[2] The present communication is an account of further unsuccessful experiments with this aim.


(I)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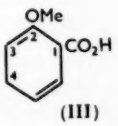
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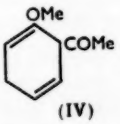

(IV)

Pinder and Smith [2] found that reduction of suitable aromatic precursors, *e.g. o*-methoxyacetophenone, by sodium and liquid ammonia led to hydrogenolysis. In reducing aromatic carboxylic acids, Birch [3] found that in general the aromatic ring was reduced in the expected manner, and the carboxyl group remained intact, being protected as its anion against hydrogenolysis. In later investigations on the reductions of substituted

* The authors are indebted to a Referee for suggesting this structure, as well as structure (IV) and the nature of the impurity in the acid (III).

[1] Cf. Peak and Robinson, *J.*, 1937, 759, 1581.

[2] Smith, *J.*, 1953, 803; Pinder and Smith, *J.*, 1954, 113; Jaeger and Smith, *Chem. and Ind.*, 1954, 1106; *J.*, 1955, 160, 646; McEntee, Pinder, Smith, and Thornton, *J.*, 1956, 4699.

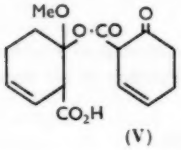
[3] Birch, *J.*, 1944, 430; 1950, 1551.

o-anisic acids,[4] although the carboxyl group was not hydrogenolysed, decarboxylation occurred immediately on hydrolysis of the dihydro-acids, and there was evidence of partial hydrogenolysis of the methoxyl group. Nevertheless, if *o*-anisic acid (II) could be reduced to the dihydro-acid (III), the latter could probably be converted into the ketone (IV) and thence, under mild conditions, into (I).

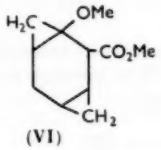
Reduction of *o*-anisic acid with sodium and methanol in liquid ammonia gave an acidic syrup which could not be purified satisfactorily owing to the ease with which it lost carbon dioxide, though it was characterised as *p*-bromophenacyl ester and *S*-benzylthiuronium salt. The compound absorbed maximally in the ultraviolet region at 240 mμ, on acid hydrolysis gave *cyclo*hex-2-enone, with elimination of carbon dioxide, and with chromic acid afforded *o*-anisic acid in high yield. These observations suggest that the product is mainly 1 : 4-dihydro-*o*-anisic acid (III).* A homoannular conjugated diene system is not present, since according to Woodward's rules such systems show maximal absorption above 253 mμ.[5a] Formulation of the acid as a βγ- rather than an αβ-unsaturated acid is further supported by the ease of decarboxylation. The observed ultraviolet maximum may be due to the presence of some 6-oxo*cyclo*hex-1-enecarboxylic acid, arising from the enol ether (III) by hydrolysis during working-up : this keto-acid might be expected to show a maximum at a relatively high wavelength for an αβ-unsaturated acid because of strain in the *cyclo*hexene ring.[5b]

At room temperature the syrupy acid gradually lost carbon dioxide and crystals separated in small yield. The new compound had a molecular weight about twice that of the syrupy acid, was enolic, and still contained a methoxyl group. The structure (V) has been tentatively assigned to it; it would be obtained by Michael addition of 6-oxo*cyclo*hex-2-enecarboxylic acid, an intermediate hydrolysis product of (III), to the enol ether double bond of (III).

When treated with an excess of diazomethane, the syrupy acid afforded an ester with a terpene-like odour, which showed no strong ultraviolet absorption and appeared to be saturated. Its analysis supported the molecular formula $C_9H_{10}O(OMe)_2$, indicating that simultaneously with esterification of the carboxyl group, two methylene groups had been added to the molecule. Further, the original methoxyl group was no longer hydrolysable to a ketone, and an infrared band at 1010 cm.$^{-1}$ suggested the presence of a *cyclo*propane ring.[6] The structure (VI) is proposed for the ester.



(V)



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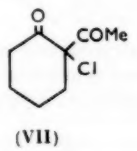

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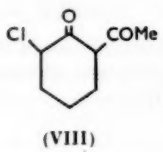


(VIII)

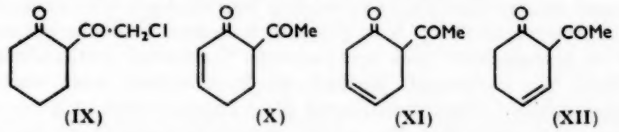
Attempts to convert the syrupy acid into the ketone (IV) by the action of methyllithium [7] gave, after hydrolysis, mainly *cyclo*hex-2-enone, with some 1-acetyl*cyclo*hexene, the latter presumably arising from the presence of a little 1 : 2 : 3 : 4-tetrahydrobenzoic acid in the syrupy acid.

Whilst these investigations were in progress, Birch, Hextall, and Sternhell [8] reported some further experiments on the reduction of anisic acids. With *m*-anisic acid and *N*-methylanthranilic acid their ultimate products were respectively 3-oxo*cyclo*hexanecarboxylic acid and *cyclo*hexanone. We have not detected *cyclo*hexanone in our reduction

[4] Birch, Murray, and Smith, *J.*, 1951, 1945.
[5] (*a*) Woodward, *J. Amer. Chem. Soc.*, 1942, **64**, 72, 76; (*b*) Jones, Mansfield, and Whiting, *J.*, 1956, 4073, and references there cited.
[6] Bellamy, "The Infrared Spectra of Complex Molecules," Methuen, London, 1954, pp. 13, 27.
[7] Cf. van Dorp and Arens, *Rec. Trav. chim.*, 1946, **65**, 344; Gilman, Zoellner, and Selby, *J. Amer. Chem. Soc.*, 1933, **55**, 1252.
[8] Birch, Hextall, and Sternhell, *Austral. J. Chem.*, 1954, **7**, 256.

of *o*-anisic acid, which suggests that in the acid (III) conjugation of the double bonds does not occur readily.

Turning to 2-acetyl*cyclo*hexanone, we found that its treatment with bromine or *N*-bromosuccinimide gave polybromo-ketones which readily decomposed, as in Acheson's work with 2-acetyl*cyclo*pentanone.[9] Warnhoff and Johnson[10] used sulphuryl chloride for the formation of a tertiary α-chloro-ketone: with this reagent in carbon tetrachloride 2-acetyl*cyclo*hexanone afforded 2-acetyl-2-chloro*cyclo*hexanone (VII) in high yield. This compound was insoluble in cold, dilute alkali, gave no colour with alcoholic ferric chloride, and did not form a copper complex; its infrared absorption spectrum was not of the conjugate chelate type,[11] but was that of a non-enolisable diketone, so that possible alternative structures such as (VIII) and (IX) were eliminated.

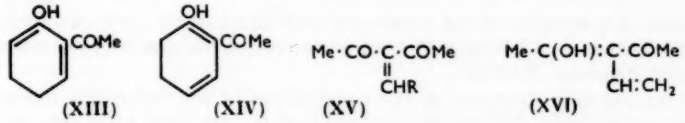


(IX) (X) (XI) (XII)

Dehydrochlorination of the chloro-ketone by collidine or by lithium chloride in dimethylformamide[12] gave two products in each case, namely, a liquid, $C_8H_{10}O_2$, and a crystalline compound, m. p. 136°, which appeared to be a dimer of the liquid.

The liquid was typically enolic in its chemical properties, being readily soluble in cold, aqueous alkali, giving a deep purple ferric test, and forming a crystalline copper complex, by means of which it could be purified. Its infrared absorption (liquid film) was of the conjugate chelate type;[11] it showed ultraviolet maxima at 240 mμ (ε 6640) and 325 mμ (ε 2600) (in MeOH), and at 238 mμ (ε 6500) and 322 mμ (ε 3300) (*cyclo*hexane). On catalytic hydrogenation it absorbed one mol. of hydrogen with the formation of 2-acetyl-*cyclo*hexanone, and on catalytic dehydrogenation or mild oxidation it yielded *o*-hydroxy-acetophenone very readily. On this evidence the compound is certainly an acetyl*cyclo*-hexenone, of structure (I), (X), (XI), or (XII), the last three being formed by double-bond migration following dehydrochlorination of (VII). The diketone[13] (X) differs in physical and chemical properties from our product. We are grateful to Dr. C. W. Smith, and the Shell Development Co., New York, for supplying unpublished additional information about the compound, which we have attempted unsuccessfully to synthesise by the reaction of *cyclo*hex-2-enone with acetyl chloride in the presence of sodamide,[14] and with acetic anhydride in the presence of boron trifluoride.[15]

The compound $C_8H_{10}O_2$, on oxidation with potassium permanganate in acetone, gave succinic acid as sole crystalline product. This eliminates structure (XI), leaving structures (I) and (XII) to be considered. It is difficult to explain the enolic behaviour of the product on the basis of formula (I). Such a compound could in theory enolise to (XIII),



(XIII) (XIV) (XV) (XVI)

but such an enolisation would in fact require additional activation of the hydrogen atoms at $C_{(6)}$ in (I), and, further, such an enol cannot be stabilised by resonance between

[9] Acheson, *J.*, 1956, 4232.
[10] Warnhoff and Johnson, *J. Amer. Chem. Soc.*, 1953, **75**, 494.
[11] Bellamy, ref. 6, p. 123.
[12] Cf. Holysz, *J. Amer. Chem. Soc.*, 1953, **75**, 4432.
[13] Smith, U.S.P. 2,516,729; *Chem. Abs.*, 1951, **45**, 6217.
[14] Cf. Conia, *Bull. Soc. chim. France*, 1954, 690, 943; 1955, 301.
[15] Hauser, Swamer, and Adams, "Organic Reactions," Vol. VIII, Chapter 3.

zwitterionic forms (cf. Smith [2]). We therefore propose structure (XII), the double bond having taken up a position of non-conjugation with both carbonyl groups. This formulation appears to explain the properties of the product satisfactorily, for enolisation would yield (XIV); spectral measurements indicate that it exists almost wholly as this form in the liquid state and in solution. The peaks at 325 mμ (in MeOH) and 322 mμ (in *cyclo*hexane) are presumably due to the enol (XIV), in which there is a homoannular conjugated diene system, with a hydroxyl substituent exerting a strong bathochromic effect (compare the enolic form of 2-acetyl*cyclo*hexanone, $\lambda_{max.}$ 290 mμ; Smith [2]).[5,16] The maxima in the 240 mμ region may probably be due to the αβ-unsaturated ketone system which is also present.[5,16]

In an attempt to support this formulation we examined the properties of several compounds based on structure (I). Condensing benzaldehyde with acetylacetone [17] gave 3-benzylideneacetylacetone (XV; R = Ph), which showed no enolic properties. Similar condensation of acetaldehyde and acetylacetone [17] afforded 3-ethylideneacetylacetone (XV; R = Me): this compound, purified, by fractionation, from unchanged acetylacetone, showed infrared absorption (liquid film) characteristic of a non-enolised β-diketone; the curves of (XV; R = Ph and Me) were indeed closely similar. However the compound gave a purplish-red colour with alcoholic ferric chloride, and dissolved slowly in aqueous alkali: shaking it with cupric acetate solution caused no immediate reaction, but the copper complex of acetylacetone was slowly obtained in high yield, owing to hydrolytic cleavage. It appears that in the liquid state the compound (XV; R = Me) exists wholly as the diketo-form, but in solution in certain solvents may enolise to a small extent to (XVI). The ultraviolet absorption in methanol solution supports this view [$\lambda_{max.}$ 220 (ε 10,600) and 285 mμ (ε 665); the latter peak is probably due to the presence of the enol form (XVI)]. It is unlikely that these properties could be due to the presence of acetylacetone as impurity, because the ferric colour is purplish-red, whereas acetylacetone gives a wine-red colour. The former colour is characteristic of enolised –CO·CHR·CO– systems, where R is alkyl.[18] Secondly, acetylacetone reacts immediately with cupric acetate, even in very low concentration; and, thirdly, acetylacetone has $\lambda_{max.}$ 272·5 mμ (in EtOH).[19] In *cyclo*hexane solution the compound (XV; R = Me) showed only a single maximum at 218 mμ (ε 12,600), so that in this solvent no appreciable enolisation occurred.

In contrast condensation of propionaldehyde and acetylacetone yields a compound $C_8H_{12}O_2$ which is completely enolic [cf. (XVIII)]. It has a typical conjugate chelate infrared spectrum, readily forms a crystalline copper complex, and gives a deep purple ferric colour. It has ultraviolet maxima at 222 (ε 15,200) and 290 mμ (ε 11,200) in methanol; in *cyclo*hexane the positions are 220 (ε 15,000) and 290 mμ (ε 11,500). These values correspond very well with those of the product $C_8H_{10}O_2$, the longer wavelengths of the maxima in the case of this compound being accounted for by the presence of a cyclic structure.

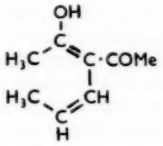
The chemical properties of the compound (XVII) resemble very closely those of one obtained by Tiemann and Krüger [20] from *iso*valeraldehyde and acetylacetone, to which they assigned structure (XVIII).

An account of investigations on the constitution of the crystalline dimer $C_{16}H_{20}O_4$, m. p. 136°, is reserved for a later communication. In our view this compound is probably a dimer of the structure (I), and its formation accounts in part for the failure to isolate the ketone (I) by the procedure described. Jones and Koch [21] have shown that 1-acetyl*cyclo*hexene dimerises to a compound (XIX); the analogous structure for the

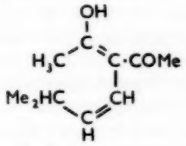
[16] Woodward, *J. Amer. Chem. Soc.*, 1941, **63**, 1123.
[17] Knoevenagel and Ruschhaupt, *Ber.*, 1898, **31**, 1026; Knoevenagel and Faber, *ibid.*, p. 2775.
[18] Henecka, *Chem. Ber.*, 1948, **81**, 179.
[19] Grossmann, *Z. phys. Chem.*, 1924, **109**, 305.
[20] Tiemann and Krüger, *Ber.*, 1895, **28**, 2121.
[21] Jones and Koch, *J.*, 1942, 393.

dimer of 2-acetyl*cyclo*hex-2-enone (I) would be (XX). This, however, cannot represent the dimer, m. p. 136°, since the infrared spectrum of the compound shows the complete absence of a non-enolisable carbonyl group, such as is present in (XX).

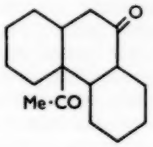
Similar studies in the *cyclo*pentane field are being pursued.



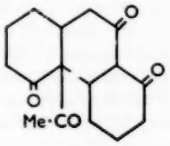
(XVII)



(XVIII)



(XIX)



(XX)

Experimental

Ultraviolet absorption measurements refer to MeOH solutions unless otherwise stated.

o-Anisic Acid.—Methylation of salicylic acid with methyl sulphate and alkali [22] gave a product contaminated with salicylic acid (even when a large excess of methyl sulphate was employed), which could not be removed by fractional crystallisation. Methyl salicylate was therefore methylated by the same procedure,[23] unchanged phenolic material being removed with alkali. Methyl *o*-anisate distilled at 128°/10 mm. (lit.,[23] b. p. 140—144°/15 mm.). The ester (96 g.) was boiled under reflux for 15 min. with 10% aqueous sodium hydroxide (400 c.c.), and the clear solution cooled and acidified with concentrated hydrochloric acid. *o*-Anisic acid was collected and crystallised from aqueous methanol. The pure acid (81 g.) had m. p. 99—100° (lit.,[23] m. p. 99—101°) and gave no colour with alcoholic ferric chloride. The *S-benzylthiuronium salt* separated from ethanol in prisms, m. p. 159° (decomp.) (Found: C, 60·3; H, 5·7. $C_{16}H_{18}O_3N_2S$ requires C, 60·4; H, 5·7%).

Reduction of o-Anisic Acid with Sodium in Liquid Ammonia.—The pure acid (10 g.) in methanol (4 c.c.) was added gradually with stirring to liquid ammonia (300 c.c.), followed by sodium (9·1 g.), in small pieces, during 1 hr. When all the sodium had dissolved ammonium chloride (50 g.) in water (120 c.c.) was added, with stirring, and the mixture left for several hours for complete evaporation of the ammonia. The clear solution was freed from neutral matter with ether, acidified with concentrated hydrochloric acid, and extracted thoroughly with ether. Evaporation of the combined, dried extracts gave a syrup (8·0 g.), which effervesced slowly, with evolution of carbon dioxide. Purification of this product proved extremely difficult, owing to the ease of decarboxylation, but its subsequent reactions indicated that it was mainly 1 : 4-dihydro-*o*-anisic acid (III) (Found: equiv., 152, 159. $C_8H_{10}O_3$ requires equiv., 154), $\lambda_{max.}$ 240 mμ (ε 2900). The *S-benzylthiuronium salt* separated from ethyl acetate–ethanol (1 : 1) in prisms, m. p. 146—147° (Found: C, 59·7; H, 6·2. $C_{18}H_{20}O_3N_2S$ requires C, 60·0; H, 6·25%), showing a large depression in m. p. when mixed with *S*-benzylthiuronium *o*-anisate. The *p-bromophenacyl ester* separated from methanol in rhombic plates, m. p. 78° (Found: C, 54·7; H, 4·6. $C_{16}H_{15}O_4Br$ requires C, 54·7; H, 4·3%).

The syrupy acid (2·0 g.) was hydrolysed by boiling N-hydrochloric acid (25 c.c.) for 30 min. The solution was neutralised with sodium carbonate and extracted with ether. Evaporation of the dried extract gave *cyclo*hex-2-enone, b. p. 53—54°/9 mm. (0·7 g.) (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 166—167°).

When the acid (4 g.) in glacial acetic acid (15 c.c.) was mixed with chromic acid (1·9 g.) in water (3 c.c.) an exothermic reaction occurred. After several hours the solution was diluted with water and extracted with ether. The dried extract was evaporated, the last traces of acetic acid being removed *in vacuo*. The residue (3·4 g.) of *o*-anisic acid crystallised from aqueous methanol in prisms, m. p. and mixed m. p. 99°.

From the syrupy acid crystals separated during several days. These recrystallised from acetic acid in prisms, m. p. 166—167° (decomp.) (Found: C, 60·7, 61·1; H, 6·0, 6·2; Me, 8·9%; *M*, 283. $C_{15}H_{18}O_6$ requires C, 61·2; H, 6·1; OMe, 10·5%; *M*, 294). The *compound* was

[22] Graebe, *Annalen*, 1905, **340**, 204.
[23] Cohen and Dudley, *J.*, 1910, **97**, 1732.

XUM

soluble in sodium hydrogen carbonate solution, with evolution of carbon dioxide; it gave a deep red colour with alcoholic ferric chloride.

Reaction of the Syrupy Acid with Diazomethane.—The acid (5 g.) in dry ether (50 c.c.) was kept with excess of an ethereal solution of diazomethane at 0° overnight; the solution was washed with sodium hydrogen carbonate solution and water, dried, and evaporated. The residual *methyl* 1-*methoxy*tricyclo[5 : 1 : 0 : $0^{3:5}$]*octane*-2-*carboxylate* (VI) distilled at 79—80°/18 mm. and had n_D^{20} 1·4600 (4·5 g.) (Found: C, 67·0, 67·5; H, 7·9, 8·25; OMe, 24·5. $C_{11}H_{16}O_3$ requires C, 67·3; H, 8·2; 2OMe, 31·6%) and no ultraviolet absorption above 215 mμ. Infrared absorption bands were at 1724 (ester C=O group), 1163 (ester group), 1075 (aliphatic ether), 1010 (*cyclo*propane ring), and 2915 cm.$^{-1}$ (methylene groups). The product had a pleasant, terpene-like odour; it was stable for several minutes to cold, aqueous potassium permanganate solution, gave no colour with ferric chloride, and did not react with 2 : 4-dinitrophenylhydrazine in the presence of sulphuric acid.

Reaction of the Syrupy Acid with Methyl-lithium.—A solution of methyl-lithium in ether [prepared from lithium metal (4·6 g.), methyl iodide (55 g.), and ether (400 c.c.); cf. van Dorp and Arens [7]] (180 c.c.; 2 mols.) was treated under nitrogen with the acid (8·5 g.) in ether (150 c.c.) during 1 hr., with stirring. After an additional hour's stirring the mixture was poured on ice, and the organic layer separated, washed with sodium hydrogen carbonate solution and water, dried, and evaporated through a short Vigreux column. The oily residue (6·2 g.) was boiled with N-hydrochloric acid (25 c.c.) under nitrogen for 1 hr. Ether-extraction of the cooled solution gave an oil (3·5 g.), which was distilled fractionally *in vacuo* through a vacuum-jacketed Vigreux column. The main fraction distilled at 57°/10 mm. (2·8 g.), having n_D^{20} 1·4799 (Found: C, 74·75; H, 8·2. Calc. for C_6H_8O: C, 74·9; H, 8·4%). The 2 : 4-dinitrophenylhydrazone separated from ethanol in deep orange needles, m. p. 164° alone or mixed with *cyclo*hex-2-enone 2 : 4-dinitrophenylhydrazone (m. p. 164—165°). The higher-boiling fraction (0·5 g.) had b. p. 92°/18 mm., n_D^{20} 1·4880 (Found: C, 77·5; H, 9·8. Calc. for $C_8H_{12}O$: C, 77·4; H, 9·7%). The 2 : 4-dinitrophenylhydrazone crystallised from ethyl acetate in bright red needles, m. p. 202—203°, undepressed by admixture with 1-acetyl*cyclo*hexene 2 : 4-dinitrophenylhydrazone (m. p. 203°).

2-*Acetyl*-2-*chloro*cyclo*hexan*-1-*one*.—Sulphuryl chloride (29·7 g., 0·22 mole) in carbon tetrachloride (50 c.c.) was added during 1 hr. to a stirred solution of 2-acetyl*cyclo*hexanone [24] (28 g., 0·2 mole) in carbon tetrachloride (100 c.c.), the temperature being kept below 20°. Stirring was continued for a further 2 hr.; the clear solution was then washed with water and saturated sodium hydrogen carbonate solution (2 × 25 c.c. each), and dried (Na_2SO_4). Evaporation of the solvent *in vacuo* through a short Vigreux column gave a reddish oil which redistilled (Vigreux column) at 50—51°/0·1 mm. (21 g.) and had n_D^{25} 1·4790 (Found: C, 54·7, 54·8; H, 6·5, 6·5; Cl, 20·5, 20·3. $C_8H_{11}O_2Cl$ requires C, 55·0; H, 6·3; Cl, 20·3%), strong carbonyl band at 1713 cm.$^{-1}$ and a C–Cl (?) band at 803 cm.$^{-1}$ (spectrum not of conjugate chelate type). 2-*Acetyl*-2-*chloro*cyclo*hexanone* had a sharp, lachrymatory odour, and solidified to elongated prisms, m. p. ~8°, insoluble in dilute, aqueous sodium hydroxide, giving no colour with ferric chloride, and not reacting with cupric acetate. With 2 : 4-dinitrophenylhydrazine in ethanol containing a few drops of concentrated sulphuric acid it gave an amorphous, orange precipitate, which did not contain chlorine. Attempts to purify this compound were unsuccessful.

Dehydrochlorination of 2-*Acetyl*-2-*chloro*cyclo*hexanone*.—(*a*) When the above chloro-ketone (5 g.) and freshly distilled dry collidine (15 c.c.) were heated, sudden reaction occurred at 180° (bath temperature) with separation of collidine hydrochloride. Heating was continued at 180° for 30 min., then the mixture was cooled, diluted with ether, and filtered. The hydrochloride was washed with ether (yield, 4·45 g.; theor., 4·51 g.), and the combined filtrate and washings were shaken in turn with dilute hydrochloric acid (3 × 30 c.c.), water, ice-cold, dilute sodium hydroxide solution (2 × 25 c.c.), and water, dried and evaporated. A dark brown oil (0·15 g.) remained which mainly decomposed when an attempt was made to distil it at 11 mm.

The alkaline extracts were acidified with 5N-hydrochloric acid, and the oil liberated was isolated with ether (yield, 3·5 g.), recovered, redissolved in ether (10 c.c.), and kept at 0° overnight. The crystals (1·0 g.) so obtained (A; see below) were collected and washed with a little ether. The filtrate was evaporated; the residue of (?) 2-*acetyl*cyclo*hex*-3-*enone* (XII), distilled *in vacuo*, had b. p. 98—99°/9·5 mm., 101—102°/10·5 mm., n_D^{25} 1·5377 (0·6 g.) (Found: C, 69·6, 69·4; H, 7·4, 7·3. $C_8H_{10}O_2$ requires C, 69·5; H, 7·3%), ultraviolet absorption max. at 240

[24] "Organic Reactions," Vol. VIII, p. 130.

(ε 6640) and 325 mμ (ε 2600) (in MeOH), 238 (ε 6500) and 322 mμ (ε 3300) (in *cyclo*hexane), and infrared absorption (conjugate chelate spectrum) bands at 3030 (shoulder), 1636, 1603, 1444, 1410, 1172, and 1146 cm.$^{-1}$. Much involatile material remained. The product formed a *copper complex* when shaken in ether with aqueous cupric acetate; this separated from benzene–light petroleum (b. p. 60—80°) (1 : 1) in greyish-green matted needles, m. p. 192° (Found: C, 57·2; H, 5·45. $C_{16}H_{18}O_4Cu$ requires C, 56·9; H, 5·3%). When shaken in ethereal suspension with dilute sulphuric acid the complex was smoothly reconverted into the product $C_8H_{10}O_2$, which was soluble in dilute sodium hydroxide solution, being precipitated on acidification. With alcoholic ferric chloride it gave a deep purple colour. Attempts to make the semicarbazone, oxime, and phenylhydrazone resulted in oils; with 2 : 4-dinitrophenylhydrazine there was obtained an amorphous orange-red compound, which when purified by chromatography on bentonite–kieselguhr gave a microcrystalline product, m. p. 248—252° (decomp.) (Found: C, 47·1; H, 3·6; N, 21·5. Calc. for bis-2 : 4-dinitrophenylhydrazone, $C_{20}H_{18}O_8N_8$: C, 49·6; H, 3·6; N, 22·5%).

(*b*) A stirred solution of lithium chloride (3·6 g.) and the chloro-ketone (5 g.) in dimethylformamide (50 c.c.) was heated at 100—110° under nitrogen for 4 hr.,[12] then cooled, poured into water (100 c.c.), and extracted with benzene (3 × 50 c.c.). The extracts were washed with cold, dilute hydrochloric acid, sodium hydrogen carbonate solution, and water, dried, and evaporated. The residue was partly crystalline and afforded the same two products as in (*a*), in similar yield.

Dimeric Product, $C_{16}H_{20}O_4$.—The deposit (A; see above) crystallised from methanol in very pale yellow rhombic prisms, m. p. 136° (0·9 g.) (Found: C, 69·4; H, 7·3; *C*-Me, 10·2%; *M*, 274. $C_{16}H_{20}O_4$ requires C, 69·6; H, 7·2; 2*C*-Me, 10·8%; *M*, 276). Ultraviolet absorption: max. at 250 (ε 14,400), 288 mμ (ε 9870). Infrared absorption (Nujol mull): typical conjugate chelate spectrum, almost complete enolisation. The *substance* was soluble in dilute sodium hydroxide solution, gave a deep blue colour with alcoholic ferric chloride, and formed a crystalline copper complex, m. p. >250°, with aqueous cupric acetate, but this did not recrystallise satisfactorily.

Dehydrogenation of $C_8H_{10}O_2$.—Palladium–charcoal (30%; 0·2 g.)[25] was added to the product $C_8H_{10}O_2$ (0·5 g.). A vigorous reaction occurred and the mixture was heated under nitrogen at 220—230° for 1 hr. After cooling, ether was added and the solution filtered. Evaporation yielded an oil which distilled at 93—94°/8 mm. (0·3 g.), had n_D^{25} 1·5520, and afforded an oxime,[26] m. p. 116—117°, and a phenylhydrazone,[27] m. p. 110—111°, both alone or admixed with the corresponding derivatives of *o*-hydroxyacetophenone. A similar product was obtained when the compound $C_8H_{10}O_2$ was boiled under reflux for several hours with dilute sodium hydroxide; no carboxylic acid was isolated.

Hydrogenation of $C_8H_{10}O_2$.—The compound (0·29 g.) in ethanol (10 c.c.) was shaken in hydrogen at room temperature and pressure with 10% palladised charcoal for 2 hr. (absorption 39 c.c.; 1 mol. = 47 c.c.). The catalyst was removed and the solvent evaporated *in vacuo*. The residual oil distilled at 97°/10 mm. (0·25 g.) (Found: C, 68·7; H, 8·6. Calc. for $C_8H_{12}O_2$: C, 68·5; H, 8·6%). Shaking it in ether with aqueous cupric acetate gave a copper complex which crystallised from ethanol in green leaflets, m. p. 162—163°, alone or mixed with an authentic specimen of the copper complex of 2-acetyl*cyclo*hexanone.[28]

Oxidation of $C_8H_{10}O_2$.—A solution of the compound (1·0 g.) in dry, permanganate-stable acetone (50 c.c.) was stirred and cooled to 0°. Finely powdered potassium permanganate was added in small quantities at a time, at 0—5°, until a permanent pink colour was obtained. After 30 minutes' further stirring, the solution was filtered and the residue washed with a little acetone and dried at room temperature. The dry solid was mixed with water (100 c.c.), and the manganese dioxide removed by filtration. The filtrate was acidified with hydrochloric acid and subjected to continuous ether-extraction for 12 hr. Evaporation of the dried extract gave succinic acid (0·3 g.), m. p. 185° (bis-*p*-bromophenacyl ester, m. p. 211°), both alone or mixed with authentic specimens.

Ozonolysis of the product $C_8H_{10}O_2$ by the method of Linstead, Elvidge, and Whalley[29]

[25] Linstead and Thomas, *J.*, 1940, 1127.
[26] Lindemann and Thiele, *Annalen*, 1926, **449**, 63.
[27] Torrey and Brewster, *J. Amer. Chem. Soc.*, 1913, **35**, 426; Bogert and Marcus, *ibid.*, 1919, **41**, 83.
[28] Borsche, *Annalen*, 1910, **377**, 88; Meerwein and Vossen, *J. prakt. Chem.*, 1934, **141**, 149.
[29] Linstead, Elvidge, and Whalley, "A Course in Modern Techniques of Organic Chemistry," Butterworths, London, 1955, pp. 116—121.

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gave, after several hours, only *o*-hydroxyacetophenone [2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 211—212° (Found: C, 53·2; H, 3·7; N, 18·2. Calc. for $C_{14}H_{12}O_5N_4$: C, 53·2; H, 3·8; N, 17·7%). Nummy and Tarbell [30] give m. p. 212—213°].

3-*Benzylideneacetylacetone*.—The preparation of this compound has been described only very briefly.[17] Benzaldehyde (10·6 g.) and acetylacetone (10·0 g.) were mixed and cooled to −10°, and piperidine (1 c.c.) was added dropwise during a few minutes. The reaction was allowed to proceed at 0° for 3 days. The turbid mixture was diluted with ether and washed in turn with dilute hydrochloric acid, dilute sodium hydroxide, and water. The dried ethereal solution was evaporated. The residual 3-benzylideneacetylacetone had b. p. 168—170°/13 mm. (12·5 g.) (lit.,[17] b. p. 179—181°/12 mm.). Ultraviolet absorption: max. at 282 mμ (ε 19,700). Infrared absorption (liquid film): strong carbonyl bands at 1650 and 1703 cm.$^{-1}$; C=C band (?) at 1610 cm.$^{-1}$; no evidence of enolisation. The product was insoluble in dilute aqueous alkali, did not give a colour with ferric chloride, and did not react with aqueous cupric acetate.

3-*Ethylideneacetylacetone*.—Acetaldehyde (11·0 g.) and acetylacetone (25·0 g.) were condensed in chloroform in the presence of dry hydrogen chloride.[17] The product was fractionated twice through a 25 cm. Vigreux column. The fraction, b. p. up to 80°/10 mm. (8·5 g.), was mainly unchanged acetylacetone; the fraction, b. p. 80—81°/10 mm. (14·0 g.) (Found: C, 66·5; H, 7·8. Calc. for $C_7H_{10}O_2$: C, 66·7; H, 7·9%), was a colourless liquid with a pungent odour, ultraviolet absorption max. at 220 mμ (ε 10,600) and 285 mμ (ε 665); 218 mμ (ε 12,600) (in *cyclo*hexane), and an infrared absorption (liquid film) curve very similar to that of 3-benzylideneacetylacetone (see above) [strong carbonyl bands at 1660 and 1733 cm.$^{-1}$; C=C band (?) at 1630 cm.$^{-1}$; no evidence of enolisation].

Condensation of Propionaldehyde and Acetylacetone.—Similarly propionaldehyde (16·0 g.) and acetylacetone (25·0 g.) in chloroform (200 c.c.) gave a fraction, b. p. up to 86°/17 mm. (8·0 g.), chiefly acetylacetone, and a fraction, b. p. 88—93°/17 mm. (mainly 89—90°) (13·0 g.) which, refractionated several times, had b. p. 82°/14 mm. (11·5 g.) (Found: C, 68·5; H, 8·8. $C_8H_{12}O_2$ requires C, 68·6; H, 8·6%) and ultraviolet absorption max. at 222 (ε 15,200) and 290 mμ (ε 11,200) (in MeOH), 220 (ε 15,000) and 290 mμ (ε 11,500) (in *cyclo*hexane), and its infrared absorption (liquid film) was a typical conjugate chelate spectrum of a highly enolised compound. The product 3-*acetylhex*-3-*en*-2-*one*, was immediately soluble in dilute aqueous alkali and gave a deep purple colour with ferric chloride and a *copper complex*, dark green needles (from benzene), m. p. 188° (decomp.) (Found: C, 56·0; H, 6·5. $C_{16}H_{22}O_4Cu$ requires C, 56·2; H, 6·4%).

We are grateful to Professor R. A. Raphael, Dr. Herchel Smith, and Dr. B. R. Brown for much helpful discussion, to Dr. G. Eglinton (University of Glasgow) for the measurement and interpretation of the infrared absorptions, and to Imperial Chemical Industries Limited, Dyestuffs Division, for gifts of chemicals.

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[*Received, June 5th*, 1957.]

[30] Nummy and Tarbell, *J. Amer. Chem. Soc.*, 1951, **73**, 1500.

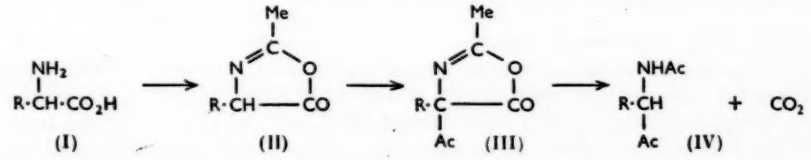
XUM

892. *The Dakin–West Reaction. Part II.* Secondary Amino-acids.*

By G. L. Buchanan, S. T. Reid, R. E. S. Thomson, and E. G. Wood.

N-Phenylglycine and a number of related compounds have been converted into derivatives of anilinoacetone by boiling them with acetic anhydride. The mechanism of the reaction is discussed, and the failure of the *N*-formyl derivative to undergo the reaction reported.

It is known [1] that most primary α-amino-acids are fairly readily converted into α-acetamido-ketones by acetic anhydride and pyridine at 100° (*e.g.* I ⟶ IV). The reaction is commonly held [2–5] to proceed by the mechanism originally suggested by Dakin and West.[6] Their suggestion is based on experiments with representative amino-acids, and in particular, on their claim [1] that the secondary, and the αα-disubstituted primary α-amino-acids which



they examined, did not so react. Their mechanism accommodates all their facts and has been supported by later investigations,[2,3,7] although it involves a final step which is not explained. The reaction has also been applied to some tertiary amino-acids,[8] and non-amino-acids (*e.g.* phenylacetic [1] and *o*-chlorophenoxyacetic acid [9]) although here a different mechanism must operate.

Wiley and Borum [10] have recently reported that under more drastic conditions sarcosine (V) yields the ketone (IX), and since then, other secondary amino-acids have been shown to react similarly.[11,12] As the oxazolone mechanism is clearly inapplicable to secondary amino-acids, we have re-investigated the mechanism, basing our studies on *N*-phenylglycine (VI). This acid, or its acetyl derivative, is readily converted into the ketone (X) by boiling acetic anhydride and pyridine: the same product is obtained by the

Ac *p*-NO_2·C_6H_4·N·CH_2·CO_2H (VIII)	R·NH·CH_2·CO_2H (V) R = Me (VI) R = Ph (VII) R = *p*-MeO·C_6H_4	Ac R·N·CH_2·Ac (IX) R = Me (X) R = Ph (XI) R = *p*-MeO·C_6H_4	COEt Ph·N·CH_2·CO·Et (XII)

action of acetic anhydride alone. When acetic anhydride was replaced by propionic anhydride the *N*-propionyl ethyl ketone (XII) was obtained. The presence of nuclear substituents had no obvious effect: *N*-*p*-methoxyphenylglycine (VII) and *N*-*p*-nitrophenylaceturic acid (VIII) reacted similarly, the former giving the methoxy-ketone (XI)

* The paper, *J.*, 1952, 2944, is considered to be Part I of this series.

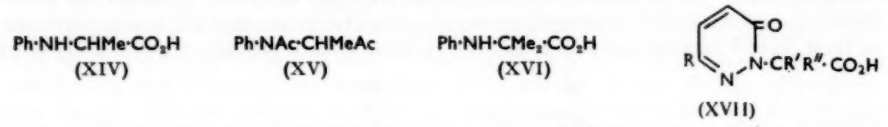
[1] Dakin and West, *J. Biol. Chem.*, 1928, **78**, 91.
[2] Cleland and Niemann, *J. Amer. Chem. Soc.*, 1949, **71**, 841.
[3] Attenburrow, Elliott, and Penny, *J.*, 1948, 310.
[4] Cornforth and Elliott, *Science*, 1950, **112**, 534.
[5] Wiley, *ibid.*, 1950, **111**, 259.
[6] Dakin and West, *J. Biol. Chem.*, 1928, **78**, 745.
[7] Wiley, *J. Org. Chem.*, 1947, **12**, 43.
[8] King and McMillan, *J. Amer. Chem. Soc.*, 1951, **73**, 4451.
[9] Smith, *ibid.*, 1953, **75**, 1134.
[10] Wiley and Borum, *J. Amer. Chem. Soc.*, 1950, **72**, 1626.
[11] Hinderling, Prijs, and Erlenmeyer, *Helv. Chim. Acta*, 1955, **38**, 1415.
[12] D.R.P. 152,012 (*Zentr.*, 1904, **2**, 70).

XUM

and the latter, surprisingly, the deacetylated amino-ketone (XIII) whose structure was confirmed by analyses and infrared spectra, and by its identity with the product of nitration of *N*-phenylacetamidoacetone (X).

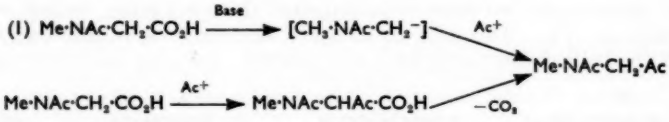
$$\text{(VIII)} \xrightarrow{Ac_2O} \underset{\text{(XIII)}}{p\text{-}NO_2\cdot C_6H_4\cdot NH\cdot CH_2\cdot CO\cdot CH_3} \xleftarrow{HNO_3} \text{(X)}$$

We examined the α-mono- and αα-di-substituted *N*-phenylglycines (XIV and XVI) to discover whether the presence of a hydrogen atom on the α-carbon was vital to the reaction. King and McMillan [13] have already demonstrated that the secondary α-acylamino-acid (XVII) is convertible into the corresponding ketone, *only* if R′ or R″ is a hydrogen atom. This shows the necessity for a free α-hydrogen atom in this series, but in view of its special

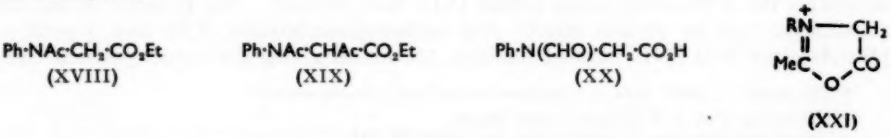


nature, it seemed advisable to examine a more conventional example. *N*-Phenylalanine (XIV) reacted with acetic anhydride, with or without pyridine, to give an oily acetamido-ketone (infrared spectrum) (XV). The disubstituted acid (XVI) yielded three products, two of which were high melting and non-ketonic, and for which no consistent analytical or infrared data could be obtained; the third was acetanilide. These findings indicate that the starting acid or the reaction product is unstable under the experimental conditions, and that the high-melting products are probably polymers.

To explain the reaction with sarcosine, Wiley and Borum [10] formulated two possible mechanisms. Neither of these can be considered satisfactory. The first is not consistent with our findings that the reaction, at least with *N*-phenylglycine, is not base catalysed, and that the acid is unaffected by boiling pyridine. The second scheme requires electrophilic substitution on the methylene group, and to test this we have investigated the



reaction of acetic anhydride and pyridine on ethyl *N*-phenylaceturate (XVIII). Here the methylene grouping should be of approximately equal activity, but the reaction should stop at the intermediate β-keto-ester stage (XIX). In fact the ester (XVIII) is recovered almost quantitatively, indicating that the true mechanism involves the carboxylic acid function *per se*.



Two further mechanisms must therefore be considered. The first, due to Cornforth and Elliott,[4] invokes the ion (XXI) [14] in place of the oxazolone (II) of Dakin and West's original mechanism (*i.e.* I ⟶ IV). Secondly, the nitrogen atom may play no part in the reaction, and in this event, the mechanism would be that which obtains for phenylacetic and *o*-chlorophenoxyacetic acid.

[13] King and McMillan, *J. Amer. Chem. Soc.*, 1952, **74**, 3222.
[14] See also Lawson and Searle, *J.*, 1957, 1556.

Neither of these mechanisms adequately explains our observation that when *N*-formyl-*N*-phenylglycine (XX) was treated under standard conditions with acetic anhydride and pyridine, the starting material was recovered in 90% yield and no ketonic material could be detected.

Experimental

Dakin–West Reaction.—*N*-Phenylglycine [15] (20 g., 0·15 mole) and acetic anhydride (150 ml., 1·7 mole) were heated under reflux for 6 hr., the excess of acetic anhydride removed at reduced pressure, and the product distilled, forming a fraction (17·1 g., 67·6%), b. p. *ca.* 115°/0·15 mm. or *ca.* 135°/1 mm. This formed needles, m. p. 79—80° (from petroleum). The *p*-nitrophenylhydrazone had m. p. 182° (from alcohol). Mixtures with authentic materials [16] have the same m. p.s.

In replicate experiments reflux times of ½, 1, 4, and 8 hr. were used. In the first case the yield was 40% and some *N*-phenylaceturic acid was recovered; in the others the yields (crude) were 53, 61, and 67%, respectively. One experiment, in which the purified *N*-acetyl derivative was refluxed for 1 hr., gave a crude yield of 65%: in another, in which pyridine (0·6 mole) was included, the same product was obtained.

After being boiled under reflux for 7 hr. with an excess of pyridine, *N*-phenylglycine was recovered in 90% yield.

1-(*N*-*phenylpropionamido*)*butan*-2-*one* (XII). *N*-Phenylglycine (10 g.) and propionic anhydride (90 ml.) were boiled under reflux for 4 hr. yielding the ethyl ketone (7·0 g., 55%), b. p. 125—130°/0·4 mm.; ν (thin film) 1723 and 1660 cm.$^{-1}$ [*oxime*, m. p. 125° (from ethanol) (Found: C, 66·4; H, 7·4; N, 12·0. $C_{13}H_{18}O_2N_2$ requires C, 66·6; H, 7·7; N, 12·0%)].

N-p-*Methoxyphenylacetamidoacetone* (XI). *N*-*p*-Methoxyphenylglycine [17] (12 g.) and acetic anhydride (75 ml.) were refluxed for 1 hr., giving the *acetamido-ketone* (45%), b. p. 136—138°/0·1 mm.; ν (thin film) 1715 and 1660 cm.$^{-1}$ [*oxime*, m. p. 118—119° (from water) (Found: C, 61·1; H, 6·7; N, 11·4. $C_{12}H_{16}O_3N_2$ requires C, 61·0; H, 6·8; N, 11·9%)].

N-p-*Nitrophenylaceturic acid* (VIII). *N*-Phenylaceturic acid (7·2 g.) in concentrated sulphuric acid (10 ml.) was cooled in ice, and concentrated nitric acid (2 ml.)–concentrated sulphuric acid (1·5 ml.) was added at <10°. After 40 min. at room temperature the solution was poured on ice. The solid product (90%) (from acetic acid) had m. p. 191° (lit.,[12] m. p. 191—192°).

N-p-*Nitroanilinoacetone* (XIII). (*a*) *N*-*p*-Nitrophenylaceturic acid (20·7 g.) and acetic anhydride (110 ml.) were refluxed for 1 hr., yielding the *ketone* (3·7 g., 22%), b. p. 130—135°/0·3 mm., m. p. 151° (from ethanol); ν (Nujol) 3350 (N–H) and 1715 (C=O) cm.$^{-1}$, no amide C=O absorption (Found: C, 55·9; H, 5·1; N, 14·6. $C_9H_{10}O_3N_2$ requires C, 55·7; H, 5·15; N, 14·4%).

(*b*) *N*-Phenylacetamidoacetone (7·2 g.) in acetic acid (5 ml.) and concentrated sulphuric acid (10 ml.) was nitrated with concentrated nitric acid (2 ml.)–concentrated sulphuric acid (1·5 ml.) at <10°. The solution was kept for 40 min. at room temperature and poured on ice. The product, m. p. 151° (from ethanol), was identical (mixed m. p. and infrared spectrum) with that described above.

2-N-*Phenylacetamidobutan*-3-*one* (XV). *N*-Phenylalanine [18] (5·5 g.), acetic anhydride (37 ml.), and pyridine (37 ml.) were refluxed for 1 hr., yielding the *acetamido-ketone* (13%), b. p. 128—132°/0·2 mm.; ν (thin film) 1715 and 1660 cm.$^{-1}$ [*oxime*, m. p. 180—181° (from water) (Found: C, 65·8; H, 7·1; N, 12·6. $C_{12}H_{16}O_2N_2$ requires C, 65·45; H, 7·3; N, 12·7%)]. The same product was obtained when the pyridine was omitted.

Dakin–West Reaction with α-Anilino-α-methylpropionic Acid.—The acid [8] (20 g.) and acetic anhydride (140 ml.) were boiled under reflux for 4 hr. On cooling, a solid product separated and more was precipitated by the addition of ether (300 ml.). This product (in all 3 g.) was separated by hot acetic acid into a soluble fraction which had m. p. 285° (from acetic acid) (Found: C, 79·4, 78·7; H, 6·1, 6·0; N, 6·4, 6·5%), and insoluble material, m. p. 330° (from nitrobenzene (Found: C, 76·0, 79·1; H, 5·6, 7·4; N, 7·1, 6·4%). Neither gave ketonic derivatives.

[15] de Mouilpied, *J.*, 1905, **87**, 435.
[16] Wolff, *Annalen*, 1952, **578**, 83.
[17] Coghill and Johnson, *J. Amer. Chem. Soc.*, 1925, **47**, 184.
[18] Nastvogel, *Ber.*, 1889, **22**, 1793.

Concentration of the mother-liquor afforded acetanilide, m. p. and mixed m. p. 113°. An intractable resin was left in the distillation flask.

Reaction with the *N*-acetyl derivative (see below) gave the same mixture.

α-Methyl-α-(N-phenylacetamido)propionic Acid. α-Anilino-α-methylpropionic acid [8] was dissolved in the minimum amount of warm acetic anhydride. Excess of water was then added; the *acetyl derivative*, m. p. 175—176° (from water), slowly separated (Found: C, 65·3; H, 6·9; N, 6·5. $C_{12}H_{15}O_3N$ requires C, 65·2; H, 6·8; N, 6·3%).

Action of Acetic Anhydride and Pyridine on Ethyl N-Phenylaceturate.—The ester (40 g.), acetic anhydride (200 ml.), and pyridine (85 ml.) were refluxed for 6 hr., and low-boiling material was then distilled off at reduced pressure. The residue gave starting material (38 g.).

Action of Acetic Anhydride and Pyridine on N-Formyl-N-phenylglycine (XXII).—The acid [19] (15 g.), acetic anhydride (75 ml.), and pyridine (75 ml.) were boiled under reflux for 4 hr. and distilled. Starting material (13·5 g.), m. p. and mixed m. p. 125°, was recovered.

The authors thank Dr. V. Wolff for authentic samples of *N*-phenylacetamidoacetone and its derivatives. They are also indebted to Mr. J. M. L. Cameron and his staff for micro-analyses and to Dr. G. Eglinton and his staff for infrared spectra.

THE UNIVERSITY, GLASGOW, W.2. [*Received, June 7th*, 1957.]

[19] Vorländer and Mumme, *Ber.*, 1901, **34**, 1647.

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893. α-1 : 4-*Glucosans. Part VII.* The Enzymic Degradation and Molecular Structure of Amylose.*

By J. M. G. COWIE, I. D. FLEMING, C. T. GREENWOOD, and D. J. MANNERS.

Amylose, prepared in the absence of oxygen, is only partially degraded (70—80%) by purified β-amylase, but is completely degraded by the concurrent action of β-amylase and Z-enzyme. Treatment of amylose with oxygen, either during fractionation or in presence of hot alkali, does not introduce barriers to the action of these enzymes.

β-Amylolysis of potato amylose and a subfraction obtained by aqueous leaching indicates that amylose is heterogeneous.

The specificity of phosphorylase, β-amylase, and barley Z-enzyme is discussed; the last enzyme, which hydrolyses anomalous linkages in amylose, has no action on α-1 : 3-, α-1 : 4-, or α-1 : 6-glucosidic linkages, or on β-linked disaccharides.

ALTHOUGH the main features of the degradation of starch-type polysaccharides by β-amylase have been known for many years, the extent of hydrolysis of amylose and the mode of action (*i.e.*, single- or multi-chain attack) remain uncertain.[1] Recent investigations by Peat,[2] Hopkins,[3] Hassid,[4] and their collaborators have shown that, in contrast to earlier reports, *pure* β-amylase converts only *ca.* 70% of amylose into maltose. This incomplete degradation is not due to retrogradation of the substrate or to inactivation of the enzyme.[2] Since the action of β-amylase ceases when glucosidic linkages other than α-1 : 4 are encountered in the substrate, the amylose samples appear to contain a small number of anomalous linkages. Peat and his co-workers [2] believe that these linkages are structural features of the native amylose; they can be hydrolysed by a specific enzyme (Z-enzyme [5]) which occurs, together with β-amylase, in soya-beans. Unpurified β-amylase preparations

* Part VI, *J.*, 1957, 3432.

[1] For reviews see (*a*) Manners, *Ann. Reports*, 1953, **50**, 288, and (*b*) Greenwood, *Adv. Carbohydrate Chem.*, 1956, **11**, 335.

[2] Peat, Pirt, and Whelan, *J.*, 1952, 705, 714.

[3] Hopkins and Bird, *Nature*, 1953, **172**, 492.

[4] Neufeld and Hassid, *Arch. Biochem. Biophys.*, 1955, **59**, 405.

[5] Peat, Thomas, and Whelan, *J.*, 1952, 723.

from this source, therefore, degrade amylose completely. Although the nature of the anomalous linkages is not yet known, Baum, Gilbert, and Scott [6] have suggested that they are introduced into the amylose, by oxidation, during the fractionation of the starch. The specificity of Z-enzyme has not yet been determined, and has been the subject of some controversy.[2-5, 7]

The present communication describes a study of the action of β-amylase, in the presence and absence of Z-enzyme, on highly purified amyloses of high molecular weight. These amyloses, which have a degree of polymerisation ($\overline{D.P.}$) of several thousand glucose residues, were prepared by the fractionation of starch in the presence and in the absence of oxygen. The effect of oxygen and hot alkali on the β-amylolysis limit of certain amyloses has also been examined. In addition, the specificity of barley Z-enzyme has been investigated.

The β-Amylolysis Limit of Amylose.—Purified soya-bean β-amylase was caused to act on several samples of amylose, which had been prepared under neutral conditions in the presence and in the absence of oxygen. The reaction was followed by determination of the liberated maltose rather than by measurement of changes in the iodine-staining power: the latter method is less precise, and gives results which are *ca.* 5% higher than those from reducing-power measurements (see p. 4436 and ref. 2); in addition, the maltose production is independent of the mode of enzyme action (cf. ref. 8). The enzyme preparation, which was free from Z-enzyme [5] and α-amylase, gave 69—86% conversion into maltose with eight amylose samples (see Table 1). Amylose IV had a β-amylolysis limit of 99%. The low β-amylolysis limits were not due to inactivation of the enzyme, since they were unaffected by changes in initial enzyme : substrate ratio, or by addition of fresh enzyme to the digests after 24 hours' incubation.

TABLE 1. *β-Amylolysis limits of amyloses.*

Sample	Conditions of prepn.[a]	$\overline{D.P.}$	β-Amylolysis limit †			
			A	B	C	D	E
I	N_2	3,200	77	92	—	99	98
II	O_2	2,800	75	—	—	98	—
III	O_2	1,600	76	—	—	99	—
IV	N_2	1,800	99	—	—	—	—
V	N_2	2,700	86	—	—	—	—
VI	Air	1,850	73 *	86	72	95	94
VII	Air	*ca.* 1,500	69	83	75	94	94
VIII	N_2	*ca.* 1,500	77	87	74	92	93
IX	N_2	*ca.* 600	77	85	79	99	—

[a] Atmosphere during fractionation (see p. 4435).
* Crystalline sweet-potato β-amylase (free from Z-enzyme) also gave 73% conversion into maltose.
† Soya-bean β-amylase at pH 4·6 on (A) untreated amylose, and (B) amylose treated with oxygen in alkali. Barley β-amylase at pH 3·6 on (C) untreated amylose, and at pH 4·6 on (D) untreated amylose, and (E) amylose treated with oxygen in alkali.

By contrast, barley β-amylase caused 92—99% degradation of the same amylose samples, when incubated at pH 4·6. Although this enzyme preparation was free from α-amylase and maltase, previous studies [9] have indicated that amorphous barley β-amylase shows Z-enzyme activity. The complete degradation of the amylose is therefore due to the combined action of barley Z-enzyme and β-amylase. Since soya-bean Z-enzyme is inactivated at pH 3·6, our barley β-amylase preparation was incubated at this pH with four amylose samples. Only 72—79% conversion into maltose was observed, the detailed results being similar to those obtained with soya-bean β-amylase. Control experiments showed that despite the decreased stability of β-amylase itself at pH 3·6, the digests

[6] Baum, Gilbert, and Scott, *Nature*, 1956, **177**, 889.
[7] Peat and Whelan, *ibid.*, 1953, **172**, 494.
[8] Bourne and Whelan, *ibid.*, 1950, **166**, 258.
[9] Bell and Manners, *J.*, 1952, 3641.

contained sufficient β-amylase to allow the limit to be reached within 6 hr., and that this limit was unchanged when the initial enzyme concentration was increased five-fold.

It appears, therefore, that barley β-amylase alone is unable to degrade amylose completely, and that barley Z-enzyme, like soya-bean Z-enzyme, is acid-labile.

Further evidence for the presence of Z-enzyme in barley was obtained by dividing a digest of amylose I and soya-bean β-amylase and adding equivalent amounts of barley and soya-bean β-amylase severally to the two portions. The addition of soya-bean enzyme had no effect; the barley preparation caused a rapid increase in the maltose content, from 77 to 98%.

The possibility that the Z-linkages may arise from changes in the physical state of the substrate, *i.e.*, "ageing," [10] has also been considered. Incubation of amylose in acetate buffer (pH 4·6) for 48 hr. at room temperature *before* the addition of barley β-amylase resulted in only a small decrease (*ca.* 8%) in β-amylolysis limit. Ageing is not therefore responsible for the resistance of some 20—30% of the amylose to pure β-amylase. Further, when digests containing soya-bean and barley β-amylase were prepared under *identical* conditions, enzyme action was complete within 2—6 hr., *i.e.*, before any appreciable ageing is likely to have taken place. (This result is substantiated by unpublished sedimentation measurements on amylose during β-amylolysis.)

The various amylose samples used in these experiments were prepared either in the presence or in the absence of oxygen, and with the exception of amylose IV (see Table 1), 14—31% of the samples was resistant to pure β-amylase. Probably, therefore, the barriers to β-amylolysis are a structural feature of the native amylose and are not introduced, by oxidation, during the *fractionation* of the starch. However, the possibility of inadvertent modification of the starch during *isolation* cannot be entirely disregarded.

The β-Amylolysis Limit of Amylose treated with Oxygen in Alkali.—Evidence suggesting that oxidation might be the source of the anomalous linkages in amylose was obtained by Gilbert and his co-workers.[6] Amylose, after treatment with oxygen at 95° in both neutral and alkaline solution, was incubated with potato phosphorylase. Only 67—81% degradation occurred whereas, under similar conditions, 90% of the original amylose was degraded (as measured by decrease in iodine-staining power). (It must be noted, however, that phosphorolysis is more accurately assayed by measurement of the production of α-D-glucosyl phosphate.) It was concluded [6] that barriers to phosphorylase action, and by analogy, to β-amylolysis, can be introduced into amylose by molecular oxygen.

We have studied the degradation, by barley β-amylase, of four amylose samples which had been heated at 98° for 20 min. in 0·5M-sodium hydroxide in a stream of oxygen. The results (Table 1) show that this treatment does not alter the percentage conversion into maltose. It follows that, under the conditions employed by Gilbert, molecular oxygen does not introduce barriers to β-amylase or Z-enzyme action.

The above experiments were repeated with pure soya-bean β-amylase, and in all instances, a small *increase* (*ca.* 10%) in β-amylolysis limit was observed. If anomalous linkages had been introduced by oxygen, then the β-amylolysis limit would *decrease*. The increase is attributed to alkaline degradation of the amylose, involving the rupture of non-terminal α-1 : 4-glucosidic linkages and the liberation of new non-reducing end-chains which are susceptible to β-amylase. The alkaline degradation, which is not detected by the combined action of β-amylase and Z-enzyme, may be followed viscometrically. In one experiment a 60% decrease in specific viscosity was observed, indicating that 1—2 α-1 : 4-glucosidic linkages per molecule had been broken. It is clear, however, that the majority of the Z-linkages in the oxygen-treated amylose are intact since the β-amylolysis limit is only 83—92%, and the residual polysaccharide is still stained blue by iodine.

Neufeld and Hassid [4] found that after dissolution of amylose β-limit dextrin in hot alkali (3 min. in 0·19N-potassium hydroxide at 100° *in air*), the polysaccharide had a

[10] Meyer, Bernfeld, Boissonnas, Gürtler, and Noelting, *J. Phys. Coll. Chem.*, 1949, **53**, 319.

β-amylolysis limit of *ca.* 50%. Dissolution of the same dextrin in hot water resulted in an increase of only 5% in β-amylolysis limit. In view of our results, it is probable that alkaline degradation of α-1 : 4-glucosidic linkages rather than Z-linkages is responsible for the increased susceptibility of the limit dextrin to β-amylase.

Comparison of our results with those of Gilbert [6] suggests that β-amylase and phosphorylase differ slightly in specificity. Phosphorolysis of an amylose chain, in which successive α-1 : 4-glucosidic linkages are broken, appears to be arrested when an "oxidised" glucose residue is encountered. In contrast, β-amylase action, involving hydrolysis of alternate glucosidic linkages, is not limited by such residues. Although the nature of the oxidised residue is not known (oxidation at $C_{(3)}$ or $C_{(6)}$ is most likely [1b]), it must differ only slightly from a normal α-1 : 4-linked glucopyranose residue since β-amylase itself has a relatively high degree of specificity.

It will be noted that amylose from two varieties of potato starch, and from wrinkled pea starch, behave in the same way towards β-amylase, Z-enzyme, and oxygen in hot alkali. The above results may, therefore, be typical of the amyloses of plant starches. It is of interest that sago, tapioca, maize, and potato amyloses are similarly degraded by β-amylase and soya-bean Z-enzyme,[2] whilst Neufeld and Hassid [4] have reported that amyloses from seven different sources are incompletely hydrolysed by pure β-amylase.

The Heterogeneity of Potato Amylose.—Several workers have reported that amylose is heterogeneous.[1b] Neufeld and Hassid [4] showed that subfractions of potato and maize amylose had different β-amylolysis limits. Meyer *et al.*[10] have reported $\overline{D.P.}$'s of 200 and 700 for two fractions obtained by aqueous leaching of potato starch, and Hopkins and Bird [3] found that similar fractions had β-amylolysis limits of 80 and 64%.

We found (see Table 2) that aqueous leaching at 70° extracts *ca.* 40% of the amylose from the granule. This fraction (amylose IV) has a $\overline{D.P.}$ of 1800, and it must be linear since it is completely degraded by purified β-amylase. In contrast, amylose I, which represents the whole amylose in the potato starch, has a $\overline{D.P.}$ of 3200 and a β-amylolysis limit of only 77%. It follows that the residual amylose remaining after aqueous leaching has a $\overline{D.P.}$ of 5000—6000 and a β-amylolysis limit of 50—60%. Aqueous extraction of the granules at 100° gives a polysaccharide (amylose V) with properties intermediate between those of amylose I and IV. The presence of the small proportion of anomalous linkages is therefore confined to the amylose fractions of higher molecular weight. Moreover, the anomalous linkages are situated, on the average, near the centre of these molecules, and not near the non-reducing end.

The Specificity of Z-enzyme and the Nature of the Anomalous Linkages.—Peat, Thomas, and Whelan [5] originally isolated Z-enzyme from a soya-bean β-amylase preparation as a stable powder which was free from glycerophosphatase and amylase activity, and with the general properties of a group-specific β-glucosidase. The fact that almond emulsin (a mixture of β-glucosidases) also showed Z-enzyme activity supported this suggestion. However, a later investigation by Neufeld and Hassid [4] showed that the laminarinase, cellobiase, and Z-enzyme activities of almond emulsin were due to distinct enzymes.

In an attempt to determine the specificity of barley Z-enzyme, the action of β-amylase (soya-bean at pH 4·6 or barley at pH 3·6) and that of β-amylase plus Z-enzyme (barley at pH 4·6) on various carbohydrates have been compared. This method of investigation is, however, limited by the availability of suitable substrates, since the action of a carbohydrase is dependent on (*a*) the specificity for the glycosidic linkage, (*b*) the nature of adjacent glycosidic linkages, and (*c*) steric factors arising from the size and shape of the substrate. For example, R-enzyme,[11] which is specific for α-1 : 6-glucosidic linkages, cannot hydrolyse isomaltose, panose, or the α-1 : 6-inter-chain linkages in glycogen and in the interior of amylopectin. The above requirements are satisfied only by the inter-chain linkages in the outer regions of an amylopectin molecule. In the present study,

[11] Hobson, Whelan, and Peat, *J.*, 1951, 1451; Peat, Whelan, Hobson, and Thomas, *J.*, 1954, 4440; Peat, Whelan, and Thomas, *J.*, 1956, 3025.

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the fact that Z-enzyme does not hydrolyse a disaccharide containing a particular linkage is not, therefore, considered to be conclusive proof of non-identity with the anomalous linkage.

The possibility that Z-enzyme action could be due to traces of α-amylase has been emphasised by Hopkins and Bird,[3] although Peat *et al.*[5,7] have reported enzymic evidence against this view. However, the constancy of the molecular weight of amylose during barley β-amylolysis [12] shows clearly that random α-amylolytic action is not occurring, and that barley α-amylase and Z-enzyme must be distinct enzymes.

If oxidation of anhydroglucose residues occurred during the isolation of a linear amylose molecule (cf. ref. 6), then the barriers to β-amylase could be " oxidised " residues situated at the non-reducing end or at some position in the chain itself. Such residues could only be removed by Z-enzyme, by the hydrolysis of one of more α-1 : 4-glucosidic linkages, *i.e.*, by an amylase-type action. Since Z-enzyme is not an amylase, it follows that the anomalous linkages cannot involve oxidised glucose residues situated as above.

By similar reasoning, the tentative suggestion [13] that the anomalous linkages are glucose residues attached by a β-linkage to the non-reducing end of a linear α-1 : 4-glucosan is considered to be unlikely.

Recent studies of partial acid hydrolysis [14] have indicated that amylopectin contains a small proportion of α-1 : 3-glucosidic linkages. These linkages may arise through the action of an amylo-1 : 4 ⟶ 1 : 3-transglucosidase acting either with phosphorylase during the synthesis of linear chains, or with Q-enzyme during the amylose ⟶ amylopectin conversion. The presence of an α-1 : 3-glucosidase in Nature has also been reported.[15]

The experiments described below indicate that Z-enzyme is not an α-1 : 3-glucosidase, and that amylose samples I—IX do not contain α-1 : 3-glucosidic linkages. A comparison has been made of the action of β-amylase, in the presence and absence of Z-enzyme, on (*a*) α-dextrins produced by the salivary α-amylolysis of isolichenin [16] and (*b*) a partial acid hydrolysate of isolichenin. This polysaccharide is a linear polymer of D-glucose containing both α-1 : 3- and α-1 : 4-linkages, and should closely satisfy the structural and steric requirements of a substrate for Z-enzyme. Measurements of reducing power showed that no hydrolysis occurred within 48 hr. It is concluded that Z-enzyme has no action on either the non-terminal or the terminal α-1 : 3-glucosidic linkages, which are liberated by the enzymic or chemical degradation of isolichenin.

The barriers to β-amylase action are unlikely to be α-1 : 6-glucosidic linkages, for the following reasons: (*a*) potato amylopectin, on incubation with barley and soya-bean β-amylase, gave similar conversions into maltose (54—56%); (*b*) treatment of amylose IX with isoamylase [17] (which hydrolyses α-1 : 6-inter-chain linkages in glycogen and amylopectin) before addition of β-amylase did not cause a significant increase in β-amylolysis; and (*c*) isomaltose and panose were not hydrolysed by either β-amylase preparation.

The suggestion [5] that amylose contains a small number of β-glucosidic linkages, which are hydrolysed by Z-enzyme, has been considered, although our studies have been limited by the fact that carbohydrates containing *both* α-1 : 4- and β-glucosidic linkages are not available as model substrates. Barley Z-enzyme appears to be distinct from laminarinase and salicinase; whereas Z-enzyme is inactivated at pH 3·6, the laminarinase and salicinase activities are only partly reduced. In addition, the barley preparation had no action on cellobiose or gentiobiose, at pH 4·6, and therefore differs from the soya-bean Z-enzyme preparation.[5]

From the above studies, it is concluded that barley Z-enzyme is not an amylase, and

[12] Cowie, Fleming, Greenwood, and Manners, *Chem. and Ind.*, 1957, 634.
[13] Barker and Bourne, *Quart. Rev.*, 1953, **7**, 82.
[14] Wolfrom and Thompson, *J. Amer. Chem. Soc.*, 1956, **78**, 4116.
[15] Larner and Gillespie, *ibid.*, p. 882.
[16] Chanda, Hirst, and Manners, *J.*, 1957, 1951.
[17] Manners and Khin Maung, *Chem. and Ind.*, 1955, 950.

does not hydrolyse α-1 : 3- or α-1 : 6-glucosidic linkages; these linkages are therefore unlikely to be the barriers to β-amylase action. In addition, although barley Z-enzyme has no action on simple β-glucosides, the possibility that amylose contains a small proportion of β-glucosidic linkages remains.

Experimental

Analytical Methods.—The general methods used were as described in previous papers of this series, except that paper chromatograms were developed with ethyl acetate–pyridine–water (10 : 4 : 3) as solvent.[18] The iodine binding-power of amyloses was measured by the potentiometric-titration method described by Anderson and Greenwood.[19] Limiting viscosity numbers [η] were determined in M-potassium hydroxide and number-average $\overline{D.P.}$ values calculated [20] from $\overline{D.P.} = 7{\cdot}4[\eta]$.

Preparation of Amylose.—The methods of fractionating the potato and wrinkled pea starches are shown in Table 2.

Enzyme Preparations.—β-Amylase was isolated from soya-beans and purified by Peat, Pirt, and Whelan's method [2] in which Z-enzyme is inactivated by a short heat treatment (30 min. at 60° at pH 4·8). The purified solution had an activity of *ca.* 20,000 units/ml. when

Table 2. *Preparation of amyloses.*

Sample	Source	Fractionation procedure: Method	Ref.	Iodine affinity *
I †	Potato var. Redskin	Thymol and BuOH	20	19·5
II	,, ,,	,, ,,	21	19·5
III	,, ,,	,, ,,	21	19·5
IV ‡	,, ,,	Aq. leaching at 70°	20	19·5
V	,, ,,	Aq. leaching at 98°	20	19·5
VI	,, King Edward.	Pyridine	22	19·1
VII	,, ,,	$Al(OH)_3$ and thymol	23	15·8
VIII	,, ,,	,, ,,	23	17·0
IX	Wrinkled pea var. Laxton's Progress	Thymol and BuOH	20	18·5

* Expressed as mg. of iodine bound per 100 mg. of starch.[19]
† Yield approx. 17 g. per 100 g. of starch.
‡ Yield approx. 7 g. per 100 g. of starch.
Samples I, II, IV, and V were recrystallised from butan-1-ol under nitrogen; amylose III was recrystallised in the presence of oxygen.

tested under the conditions suggested by Hobson, Whelan, and Peat.[24] It did not reduce the iodine-staining power of amylopectin β-dextrin and contained only an insignificant trace of maltase. The properties of the barley β-amylase have been described by Liddle and Manners.[25] The stability of this enzyme was investigated by determining the activity after varying periods of incubation at pH 4·6 and 3·6:

Time of incubation (hr.)	0	5	24
Activity units,[24] at pH 4·6	138	123	85
Activity units,[24] at pH 3·6	18	9	0

Isoamylase was isolated from brewer's yeast, as described by Manners and Khin Maung.[17]

Determination of β-Amylolysis Limits.—Digests were normally prepared by incubating, at 35° in the presence of toluene, amylose (20—50 mg.), 0·2M-acetate buffer pH 3·6 or 4·6, β-amylase (*ca.* 50—100 units/mg. of amylose), and distilled water (to a final volume of 50 ml.). Dried amylose samples were moistened with ethanol, dissolved in 0·2N-potassium hydroxide, with shaking (and warming, if necessary), and then neutralised with N-hydrochloric acid (to phenolphthalein). Amylose–butanol complexes were dissolved in distilled water, as required.

[18] Whistler and Hickson, *Analyt. Chem.*, 1955, **27**, 1514.
[19] D. M. W. Anderson and Greenwood, *J.*, 1955, 3016.
[20] Cowie and Greenwood, *J.*, 1957, 2862.
[21] Cowie and Greenwood, unpublished experiments.
[22] Whistler and Hilbert, *J. Amer. Chem. Soc.*, 1945, **67**, 1161; Higginbotham and Morrison, *Shirley Inst. Mem.*, 1948, **22**, 148.
[23] Hobson, Pirt, Whelan, and Peat, *J.*, 1951, 801.
[24] Hobson, Whelan, and Peat, *J.*, 1950, 3566.
[25] Liddle and Manners, *J.*, 1957, 3432.

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The amylose concentration was determined, in triplicate, by acid hydrolysis of a portion (1 ml.) of the digest, and estimation of the liberated glucose, as described by Pirt and Whelan.[26] Portions of the digest (1—3 ml.) were removed at intervals for determination of maltose or A.V. (absorption value of the iodine complex at 680 mμ) (see Table 3). The iodine-staining method gave slightly higher β-amylolysis limits. The β-amylolysis limit of potato amylopectin was determined similarly.

TABLE 3.

Digest	Time of incubation (hr.)	1	2	4	7	24	48
Amylose VII, pH 4·6	Conversion into maltose (%)	77	85	89	—	94	94
	Decrease in A.V. (680 mμ) (%)	73	78	91	—	98	—
Amylose VII, pH 3·6	Conversion into maltose (%)	66	69	—	73	75	75
	Decrease in A.V. (680 mμ) (%)	65	74	—	79	80	80

Action of Varying Amounts of Barley and Soya-bean β-Amylase on Amylose.—Amylose I (21·8 mg.) was incubated with barley β-amylase (100 units/mg. of substrate) at pH 4·6; after 24 hours' incubation, a further 100 units of β-amylase/mg. of substrate were added to the remainder of the digest. Results were:

Time of incubation (hr.)	1	2	6	24	48
β-Amylolysis limit (%)	89	95	98	98	98

A similar experiment with amylose I (46·2 mg.) and soya-bean β-amylase (50 units/mg. of substrate) at pH 4·6 gave 77% conversion into maltose after 24 hr. The digest was divided; to portion A, fresh soya-bean β-amylase (50 units/mg. of substrate) was added, and to portion B a similar amount of barley β-amylase. After 24 hours' incubation, the β-amylolysis limits were: A, 77; B, 98%. The residue of portion A gave an intense blue colour with iodine ($\lambda_{max.}$ 660 mμ) whilst that of digest B was achroic.

In a similar experiment with amylose VIII the following results were obtained; β-amylolysis limit (24 hours' incubation with soya-bean enzyme) 77%; after addition of fresh soya-bean β-amylase, 77%; after addition of a similar amount of barley β-amylase, 92%.

The action of barley β-amylase on amylose VIII at pH 3·6 was studied; two digests were prepared containing (*a*) 150 mg. of enzyme (initial activity *ca.* 12,000 units) and (*b*) 30 mg. of enzyme (initial activity *ca.* 2400 units). Portions from digest (*a*) were deproteinised (zinc sulphate–barium hydroxide) before analysis. The β-amylolysis limits were (*a*) 73, (*b*) 75% after 24 and 48 hours' incubation.

Effect of Oxygen on the β-Amylolysis Limit.—Amylose (samples I, VI, VII, VIII, IX) (20—30 mg.), dissolved in 0·5N-sodium hydroxide (10 ml.), was heated in a stream of oxygen at 95° for 20 min. The solution was cooled, neutralised, and incorporated into digests with soya-bean or barley β-amylase. The β-amylolysis limits, determined after 24 hours' incubation, are shown in Table 1, columns B and E. No significant increase was observed when incubation was continued for a further 24 hr. The specific viscosity of amylose VIII fell from 0·40 to 0·16 during the oxygen treatment.

Effect of "Ageing" on the β-Amylolysis Limit.—Amylose I (treated with oxygen and alkali as above) (20·4 mg.) was incubated with barley β-amylase at pH 4·6; after 24 and 48 hr. 97 and 98% conversion into maltose was observed. A similar digest in which 24·5 mg. of amylose and buffer were mixed, at room temperature (17—19°), for 48 hr. before addition of the enzyme was also examined. After a further 24 hr., 92% conversion into maltose had occurred.

The experiment was repeated with amylose VII which has a β-amylolysis limit of 94%. When digests containing 19·6 mg. of amylose dried *in vacuo* at 70°, or 20·7 mg. of air-dried amylose were incubated with buffer for 48 hr. at 18°, the β-amylolysis limits were 86 and 85%. Although no retrogradation of the amyloses was visible, it is probable that, under these extreme conditions, some ageing had occurred, with a small (5—9%) lowering of the β-amylolysis limit.

Action of β-Amylases on Isolichenin Dextrins.—Isolichenin (150 mg.) was incubated with freeze-dried salivary α-amylase [25] (15 mg.) in a 50 ml. digest at 35° for 24 hr. 20 ml. portions were then incubated in 0·2M-acetate buffer (pH 4·6) with soya-bean β-amylase solution (0·1 ml.) or barley β-amylase (25 mg.) in a total volume of 25 ml. In all three digests, the apparent percentage conversion into glucose was 10. In a second experiment, in 0·1M-citrate buffer

[26] Pirt and Whelan, *J. Sci. Food Agric.*, 1951, **2**, 224.

pH 6·5 (near the pH optimum for soya-bean Z-enzyme [5]), the conversions into glucose were 10, 11, and 9% respectively.

A similar quantity of isolichenin was hydrolysed with 0·5N-sulphuric acid (10 ml.) at 98° for 45 min., to give 32% apparent conversion into glucose. Portions of the neutralised hydrolysate (3 ml.) were incorporated into 10 ml. digests containing 0·2M-acetate buffer (pH 4·6) and β-amylase. After 24 hours' incubation, 32% conversion into glucose was observed with both soya-bean and barley β-amylase.

Action of Isoamylase on Wrinkled-pea Amylose.—Amylose IX (6·9 mg.), 0·2M-acetate buffer pH 5·89 (1 ml.), water (4·5 ml.), and isoamylase (40 mg./ml.; 0·5 ml.) were incubated at 18° for 24 hr. The enzyme was inactivated by heat, the digest cooled, and β-amylase in 0·2M-acetate buffer (pH 4·6) (250 units; 2 ml.) added. The β-amylolysis limit was 77%. In a control experiment without isoamylase, the β-amylolysis limit was 75%.

Action of Barley β-*Amylase on Simple Saccharides.*—Digests containing gentiobiose, isomaltose, panose, and cellobiose (*ca.* 10 mg.) in buffer pH 4·6 (1 ml.) containing barley β-amylase (10 mg.) were incubated at 35° for 24 hr. Glucose could not be detected (paper chromatography).

Action of Barley β-*Amylase Preparation on Laminarin and Salicin.*—The laminarinase activity of the enzyme at pH 4·6 and 3·6 was determined by a method due to Anderson and Manners; [27] the activities were 13·5 and 11·1 units respectively. In similar experiments with salicin, the activities at pH 4·6 and 3·6 were 10·1 and 8·8 units respectively.

The authors are grateful to Professor E. L. Hirst, F.R.S., for his interest, to the Rockefeller Foundation for a grant, and to the Department of Scientific and Industrial Research for a maintenance allowance (to I. D. F.).

DEPARTMENT OF CHEMISTRY, UNIVERSITY OF EDINBURGH. [*Received, June 12th,* 1957.]

[27] F. B. Anderson and Manners, unpublished experiments.

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894. *The Reaction of Cyanoacetamide with* 1 : 2-*Diketones.*

By P. C. JOCELYN and A. QUEEN.

Cyanoacetamide reacts with benzil yielding the pyrrolinone (I; R = CN). Further reaction gives a substituted pyrrolidone (III; R = Ph), analogues of which are isolated when cyanoacetamide reacts with aliphatic 1 : 2-diketones.

These pyrrolidones are easily hydrolysed to the dilactones of β-acyl-β-alkyl(or phenyl)glutaric acids (VI).

Derivatives of some of these compounds are described.

ALTHOUGH cyanoacetamide condenses with 1 : 3-diketones in the presence of piperidine to yield 4 : 6-dialkyl-3-cyanopyridones,[1] the same reaction with 1 : 2-diketones does not lead to the corresponding dialkyl*iso*pyrrolones.

One molecule of benzil first condenses with one of cyanoacetamide to give a hydrate which is converted by aqueous pyridine into an anhydrous product also formed from ammonia and ethyl 3-benzoyl-2-cyanocinnamate.[2] Unlike the latter, neither of the two compounds shows the light-absorption at 6·05 μ corresponding to a ketone and no ketonic derivatives could be prepared. Moreover, the compounds dissolve in aqueous alkali from which in both cases the hydrate is precipitated on acidification.

An absorption peak at 295 mμ (or 300 mμ for the hydrate) is consistent with the presence of a cinnamoyl grouping. The anhydrous compound forms stable *O*-alkyl derivatives, a diacetate, an *N*-methyl derivative (acidic), and an *ON*-dimethyl derivative (non-acidic).

These data indicate the pyrrolinone structure (I; R = CN) in which the acid properties are due to an allylic hydroxyl group.

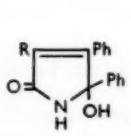
Another example of ring formation by an αβ-unsaturated γ-oxo-amide has been reported

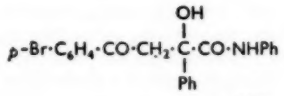
[1] Bardhan, *J.*, 1929, 2223; Weiburg and Wagtendonk, *Rec. Trav. chim.*, 1942, **61**, 728.
[2] Bacher, *J. prakt. Chem.*, 1929, **120**, 331.

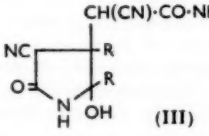
by Lutz and Hill,[3] and Bashour and Lindwall [4] have described the cyclisation of the amide (II) to the corresponding pyrrolinone with hydrogen chloride.

The cyanide group of the pyrrolinone (I; R = CN) is eliminated by alkali.

Cyanoacetamide also reacts readily with diacetyl, dipropionyl, and dibutyryl, but in these cases, two molecules of amide combine with one of diketone with loss of one of water; an analogous product is obtained from the pyrrolinone (I; R = CN) by further reaction with cyanoacetamide. These substances are non-ketonic and show no ethylenic or αβ-unsaturation. They are therefore assigned the hydroxypyrrolidone structures (III; R = Me, Et, Pr, or Ph).


(I)


(II)

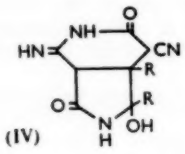

(III)

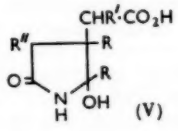
Since ammonia is not evolved from these hydroxypyrrolidones with water at 100° the cyanoacetamide residue is *trans* to the cyanide group, for if these groups were *cis*, interaction would occur [5] leading to an easily hydrolysed imino-imide (IV).[6]

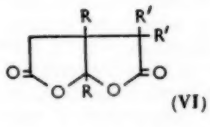
Cold 90% sulphuric acid converts (III; R = Me or Et), by addition of two molecules of water and loss of one of ammonia, into a non-ketonic acid, probably (V; R = Me or Et, R′ or R″ = CN, R″ or R′ = $CO{\cdot}NH_2$). Carbon dioxide is lost spontaneously during the attempted formation of the phenyl compound (III; R = Ph) giving a non-acidic product; the other acids are readily decarboxylated at their melting points.

When boiled with 80% sulphuric acid these acids or the amides (III) are converted into the dilactones (VI; R′ = H), a reaction which proceeds in over 90% yield for the aliphatic and in 10% yield for the phenyl compound. The aliphatic dilactones form 2 : 4-dinitrophenylhydrazones (see Emery [7]).

Fittig and Salomon [8] have prepared the dilactone (VI; R = R′ = Me) in 3% yield


(IV)


(V)


(VI)

from 1 : 1 : 2-trimethyltricarballylic (camphoronic) acid and acetic anhydride. We have failed to isolate (VI; R = Me, R′ = H) from the corresponding reaction with β-methyltricarballylic acid.

Experimental

Melting points are corrected.

4-Cyano-2-hydroxy-5-oxo-2 : 3-diphenyl-Δ³-pyrroline (I; R = CN).—Piperidine (22 g.) was added dropwise, during 15 min., to a stirred mixture of cyanoacetamide (16·7 g.), benzil (41·9 g.), and ethanol (700 ml.), and the resulting solution refluxed for ½ hr. After removal of solvent, the residue was washed with water and crystallised from aqueous ethanol yielding the *hydrate* (31·7 g.), m. p. 170°, of (I; R = CN) (Found: C, 69·9; H, 4·7; N, 9·4. $C_{17}H_{12}O_2N_2,H_2O$ requires C, 69·4; H, 4·8; N, 9·5%). Light absorption, $\lambda_{max.}$ 300 mμ (ε 6800) in ethanol.

Recrystallisation of the hydrate from aqueous pyridine gave the anhydrous *product*, m. p.

[3] Lutz and Hill, *J. Org. Chem.*, 1941, **6**, 175.
[4] Bashour and Lindwall, *J. Amer. Chem. Soc.*, 1935, **57**, 178.
[5] Thorpe and Kon, *J.*, 1919, **115**, 686.
[6] Curtis, Day, and Kimmins, *J.*, 1923, **123**, 3131.
[7] Emery, *Annalen*, 1897, **295**, 123.
[8] Fittig and Salomon, *ibid.*, 1901, **314**, 92.

186° (Found: C, 73·6; H, 4·7; N, 9·9. $C_{17}H_{12}O_2N_2$ requires C, 73·9; H, 4·4; N, 10·1%). Light absorption, $\lambda_{max.}$ 295 mμ (ε 11,000) in ethanol. Both compounds show a peak at 5·85 μ (in Nujol) (ethyl 3-benzoyl-2-cyanocinnamate shows peaks at 5·85 and 6·05 μ).

(ii) Ethyl 3-benzoyl-2-cyanocinnamate (1 g.), ethanol (30 ml.), and ammonia (*d* 0·88; 7 ml.) were kept for 4 hr. at 70° and then concentrated; the anhydrous product crystallised and had m. p. 186° undepressed on admixture with a specimen prepared as above.

The hydrate was refluxed with (i) methanol and (ii) ethanol, both containing 10% of hydrogen chloride; after evaporation of the solvent and crystallisation of the residue from ethanol, there were obtained (i) the O-*methyl* derivative, m. p. 194° (Found: C, 74·3; H, 5·0; N, 9·2. $C_{18}H_{14}O_2N_2$ requires C, 74·5; N, 4·8; N, 9·7%), and (ii) the O-*ethyl* derivative, m. p. 184° (Found: C, 74·7; H, 5·3; N, 9·0. $C_{19}H_{16}O_2N_2$ requires C, 75·0; H, 5·3; N, 9·2%).

4-Cyano-2-hydroxy- and 4-Cyano-2-methoxy-1-methyl-5-oxo-2 : 3-diphenyl-Δ³-pyrroline.—Prepared from aqueous sodium hydroxide (1·32 g. in 20 ml.), the hydrate of (I; R = CN) (2·9 g.), and dimethyl sulphate (7·6 g.) at room temperature the precipitated *2-methoxy-pyrrolinone* formed needles (2·1 g.), m. p. 158° (from 60% aqueous ethanol) (Found: C, 75·0; H, 5·4; N, 8·9; OMe, 12·9. $C_{19}H_{16}O_2N_2$ requires C, 75·0; H, 5·3; N, 9·2; OMe, 10·2%). On acidification of the combined filtrate and washings with 10% sulphuric acid, the *2-hydroxy-pyrrolinone* was precipitated; it formed needles (0·8 g.), m. p. 222° (from 60% aqueous ethanol) (Found: C, 74·0; H, 4·6; N, 9·5; OMe, 2·8. $C_{18}H_{14}O_2N_2$ requires C, 74·5; H, 4·8; N, 9·7; OMe, nil %).

2-Acetoxy-1-acetyl-4-cyano-5-oxo-2 : 3-diphenyl-Δ³-pyrroline. The hydrate of (I; R = CN) (2·0 g.) was refluxed for 10 min. with acetic anhydride (6·0 g.) in pyridine (20 ml.). After concentration at 100°/10 mm., the residue was dissolved in 70% acetone; the *product* (1·5 g.) had m. p. 159° (from 70% acetone) (Found: C, 70·2; H, 4·4; N, 7·8. $C_{21}H_{16}O_4N_2$ requires C, 70·0; H, 4·4; N, 7·8%).

2-Hydroxy-5-oxo-2 : 3-diphenyl-Δ³-pyrroline (I; R = H). The hydrate of (I; R = CN) (1 g.) was refluxed for 2 hr. with 15% sodium hydroxide solution (20 ml.), and the mixture then cooled and acidified with dilute hydrochloric acid. The *product* was isolated by ether; it slowly solidified and was crystallised from 50% aqueous ethanol forming plates (0·7 g.), m. p. 141° (Found: C, 76·3; H, 5·4; N, 5·2. $C_{16}H_{13}O_2N$ requires C, 76·5; H, 5·2; N, 5·6%).

2 : 3-Disubstituted 4-Cyano-3-cyanoacetamido-2-hydroxy-5-oxopyrrolidines (III).—To a stirred solution of cyanoacetamide (20 g.) in ethanol (150 ml.) at 55—60°, the diketone (0·125 mole) was added during ½ hr., stirring continued for a further 2 hr., and the mixture left for 12 hr. The precipitate was collected, washed with ethanol, and recrystallised as indicated. The following derivatives were prepared: *2 : 3-dimethyl* (90%) (from water), m. p. 289° (Found: C, 50·8; H, 5·3; N, 24·0. $C_{10}H_{12}O_3N_4$ requires C, 50·8; H, 5·1; N, 23·8%); *2 : 3-diethyl* (49%) (from glycol), m. p. 325—326° (Found: C, 54·3; H, 6·0; N, 21·0. $C_{12}H_{16}O_3N_4$ requires C, 54·6; H, 6·1; N, 21·2%); *2 : 3-dipropyl* (8·5%) (prepared by using water not ethanol as solvent; crystallised from glycol), m. p. 343° (Found: C, 57·8; H, 7·0; N, 19·1. $C_{14}H_{20}O_3N_4$ requires C, 57·5; H, 6·8; N, 19·1%).

The *2 : 3-diphenyl* derivative (5·3%), obtained by substituting the hydrate of (I; R = CN) (0·25 mole) for a diketone and refluxing the reaction mixture for 80 hr., was purified by successive washings with boiling ether, acetone, ethanol, and water; it had m. p. 426° (Found: C, 66·7; H, 4·5; N, 15·1. $C_{20}H_{16}O_3N_4$ requires C, 66·7; H, 4·4; N, 15·5%).

2 : 3-Disubstituted 3-Carboxyacetamido(or carboxycyanomethyl)-4-cyano(or amido)-2-hydroxy-5-oxopyrrolidines (V; R′ = CN or CO·NH₂, R″ = $CONH_2$ or CN).—The amide (III; R = Me or Et) (1 g.) in 90% sulphuric acid (11·5 ml.) was kept for 24 hr., then diluted with ice–water (30 ml.) and left for a further 36 hr. The deposited crystals were collected; the following were thus prepared: *2 : 3*-dimethyl derivative (75%), m. p. 334° (from water) (Found: C, 47·1; H, 5·4; N, 16·6. Calc. for $C_{10}H_{13}O_5N_3$: C, 47·1; H, 5·1; N, 16·5%); and *2 : 3*-diethyl derivative (25%), m. p. 337—338° (from aqueous glycol) (Found: C, 51·0; H, 6·0; N, 14·6. Calc. for $C_{12}H_{17}O_5N_3$: C, 50·9; H, 6·0; N, 14·8%).

By this method the diphenylpyrrolidone (III; R = Ph) gave 3-acetamido(or cyanomethyl)-4-cyano(or amido)-2-hydroxy-5-oxo-2 : 3-diphenylpyrrolidine (51%), m. p. 338° (from glycol) (Found: C, 68·1; H, 5·1; N, 12·4. Calc. for $C_{19}H_{17}O_3N_3$: C, 68·1; H, 5·1; N, 12·5%).

Dilactones of β-Acyl-β-alkyl(or phenyl)glutaric Acids.—The corresponding pyrrolidone (III) was refluxed for 24 hr. with 8N-sulphuric acid (20 ml.). On cooling, the product separated and was crystallised from water. Thus were prepared the *dilactones* of: β-acetyl-β-methylglutaric

acid (95%), m. p. 148° (Found: C, 56·5; H, 5·8. $C_8H_{10}O_4$ requires C, 56·5; H, 5·9%) [2 : 4-*dinitrophenylhydrazone*, m. p. 256° (Found: C, 48·0; H, 3·8; N, 15·7. $C_{14}H_{14}O_7N_4$ requires C, 48·0; H, 4·0; N, 16·0%)]; β-*ethyl*-β-*propionylglutaric acid* (95%), m. p. 100° (Found: C, 60·5; H, 7·3. $C_{16}H_{14}O_4$ requires C, 60·6; H, 7·1%); β-*butyryl*-β-*propylglutaric acid* (90%), m. p. 88—89° (Found: C, 63·9; H, 7·8. $C_{12}H_{18}O_4$ requires C, 63·7; H, 8·0%) [2 : 4-*dinitrophenylhydrazone*, m. p. 235—238° (Found: C, 52·8; H, 5·4; N, 14·3. $C_{18}H_{22}O_7N_4$ requires C, 53·2; H, 5·4; N, 13·8%]; and β-*benzoyl*-β-*phenylglutaric acid* (10%), m. p. 203—204° (Found: C, 73·3; H, 4·9. $C_{18}H_{14}O_4$ requires C, 73·4; H, 4·8%).

We are grateful to Dr. F. B. Strauss, Oxford, and Mrs. Taylor, Beecham Research Laboratories, for the infrared and ultraviolet spectrum determinations. One of us (A. Q.) is indebted to Durham County Education committee for a grant.

UNIVERSITY SCIENCE LABORATORIES, DURHAM. [*Received, April 24th,* 1957.]

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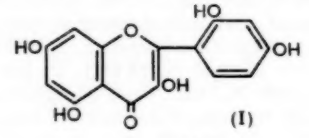
895. *Dihydromorin from East African Mulberry* (Morus lactea *Mildbr.*).

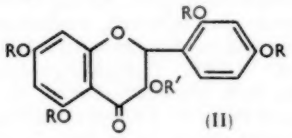
By (MRS.) W. R. CARRUTHERS, R. H. FARMER, and R. A. LAIDLAW.

A crystalline compound isolated from the heartwood of *Morus lactea* has been identified as the hitherto unknown 3 : 5 : 7 : 2′ : 4′-pentahydroxyflavanone (dihydromorin).

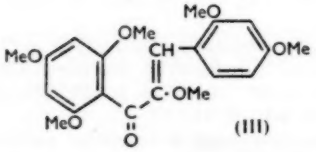
Morus lactea (East African mulberry) is fairly widely distributed in Uganda and occurs also, though only rarely, in Kenya and Tanganyika. The tree has a bole 20—40 feet long and seldom exceeds 6 feet in girth. The timber used in the present investigation was obtained from the Forest Department of Uganda for steam-bending tests, and interest in its extractives first arose when it was observed that, on steaming, the heart-wood became deep yellow throughout. The staining material, which was not found in unsteamed wood, was identified as morin (3 : 5 : 7 : 2′ : 4′-pentahydroxyflavone) (I).



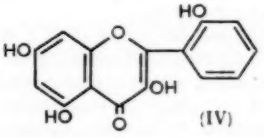
(I)



(II)



(III)



(IV)

A second crystalline compound, isolated from both steamed and unsteamed wood, readily yielded morin on aerial oxidation in aqueous solution,[1] and this, together with elementary analyses, colour reactions, and ultraviolet absorption data [2-5] (see Figs. 1 and 2) indicated that the compound was dihydromorin (3 : 5 : 7 : 2′ : 4′-pentahydroxyflavanone) (II; R = R′ = H).

Acetylation yielded a penta-acetate, confirming the presence of five hydroxyl groups, four of which were shown to be phenolic by the formation of a tetramethyl ether (II;

[1] Pew, *J. Amer. Chem. Soc.*, 1948, **70**, 3031.
[2] Skarzynski, *Biochem. Z.*, 1939, **301**, 150.
[3] Hergert, Coad, and Logan, *J. Org. Chem.*, 1956, **21**, 304.
[4] Geissman and Lischner, *J. Amer. Chem. Soc.*, 1952, **74**, 3001.
[5] Hillis, *Austral. J. Sci. Res.*, 1952, **5**, *A*, 379.

R = Me, R′ = H) and its monoacetate (II; R = Me, R′ = Ac). Treatment of dihydromorin with diazomethane produced a mixture of partly methylated derivatives. Low-temperature methylation under strongly alkaline conditions gave a product (H) which was similar to the hexamethoxychalkone prepared [3] from dihydroquercetin and may be 2 : 2′ : 4 : 4′ : 6′ : α-hexamethoxychalkone (III). This material was not examined further at this stage.

It has been shown elsewhere [6] that a chalkone with a 6′-methoxyl group lacking a hydroxyl in the 2- or 4-position gives mainly aurone, and not a flavonol or dihydroflavonol, on alkaline peroxide oxidation. In order to avoid this difficulty, the preparation of 2 : 2′ : 4-trihydroxy-4′ : 6′-dimethoxychalkone as an intermediate for the synthesis of the corresponding dihydroflavonol was attempted, but without success. Formation of the known 2′-hydroxy-2 : 4 : 4′ : 6′-tetramethoxychalkone [7] proceeded smoothly, however, and alkaline peroxide oxidation of this material gave dihydro-5 : 7 : 2′ : 4′-tetra-*O*-methylmorin in small yield, thus confirming the structure of dihydromorin. The synthetic product was slightly impure and appeared to contain some tetra-*O*-methylmorin, which probably prevented the ready formation of a crystalline acetate. No attempt was made to isolate any aurone formed during the oxidation (cf. Geissman and Fukushima [6]).

Treatment of morin with alkaline dithionite under a variety of conditions [1,4,8] failed to produce any appreciable amount of dihydromorin, whereas quercetin [1,4] and kæmpferol [5] are readily reduced by this method to their dihydro-derivatives. This anomaly may be due to some steric effect associated with the 2′-hydroxyl group, particularly as datiscetin (5 : 7 : 2′-trihydroxyflavonol) (IV) also resisted reduction.

FIG. 1. FIG. 2.

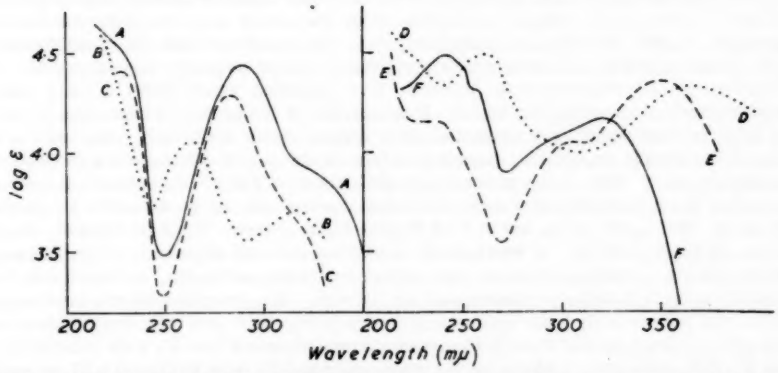


FIG. 1. *Absorption spectra of* (*A*) *dihydromorin,* (*B*) *dihydromorin penta acetate, and* (*C*) *dihydro-*5 : 7 : 2′ : 4′*-tetra-*O*-methylmorin.*

FIG. 2. *Absorption spectra of* (*D*) *morin,* (*E*) *methylated product* (*H*)*, and* (*F*) *penta-*O*-methylmorin.*

Dr. C. H. Lea, of the Low Temperature Research Station, Cambridge, finds that dihydromorin has no appreciable antioxidant activity,[9] in accord with expectation.

Several naturally occurring and synthetic dihydroflavonols are known [10] but the identification of dihydromorin in *Morus lactea* is of special interest, as this is the first example of a dihydroflavonol containing a 2′-hydroxyl group yet isolated. Further, the

[6] Geissman and Fukushima, *J. Amer. Chem. Soc.*, 1948, **70**, 1686; Anand, Iyer, and Venkataraman, *Proc. Indian Acad. Sci.*, 1949, **29**, *A*, 203; Simpson and Whalley, *J.*, 1955, 166.
[7] Kostanecki and Tambor, *Ber.*, 1904, **37**, 792.
[8] Shimizu and Yoshikawa, *J. Pharm. Soc. Japan*, 1952, **72**, 331.
[9] Lea and Swoboda, *Chem. and Ind.*, 1956, 1426; Simpson and Uri, *ibid.*, p. 956.
[10] Gowan, Philbin, and Wheeler, "The Chemistry of Vegetable Tannins: A Symposium held at Cambridge, 1956," Society of Leather Trades' Chemists, Croydon, 1956, p. 133.

unsteamed timber contained no appreciable amount of morin, though this compound has been reported [11] to be present in other timbers of the family Moraceae (*Chlorophora tinctoria, Maclura pomifera, Artocarpus integrifolia, Morus alba*).

Experimental

The wood, obtained from the Uganda Forest Department, was received as pieces 2″ × 3″ × 3′ which had been steamed and bent. Only a very small amount of unsteamed wood was available. The pale yellow heartwood alone was used for extraction, it being readily distinguishable from the pale sapwood which was shown to contain little or no dihydromorin.

Paper chromatography was carried out on Whatman's No. 1 paper by the descending method, and the following solvent systems [12] were used: (A) 15% aqueous acetic acid; (B) butan-1-ol–acetic acid–water (4 : 1 : 5) (unbuffered); (C) 22% aqueous *iso*propyl alcohol. The positions of the spots on the chromatogram were established by examination under ultraviolet light, morin giving a yellow fluorescent spot and dihydromorin a brown spot, and also by spraying with diazotised *p*-nitroaniline,[13] morin giving a brown colour and dihydromorin a bright orange-brown colour. R_F values were calculated from the distance travelled by the forward edge of the spot, as revealed under ultraviolet light.

Authentic morin, obtained from L. Light and Co. Ltd., contained small amounts of impurities which were removed by extraction with boiling water, followed by recrystallisation from dilute acetic acid. The product appeared to be chromatographically homogeneous.

Ultraviolet absorption spectra were determined in methanol solution in a Unicam S.P. 500 spectrophotometer.

The light petroleum used throughout had b. p. 60—80°, unless otherwise stated.

Extraction of Morin.—Sawdust from the steamed wood was extracted with water and morin precipitated from the extract as the lead salt.[14] The precipitate was decomposed, and the product, after recrystallisation from aqueous ethanol, was purified by passage through a column of cellulose [15] (solvent A). Morin crystallised from the eluate as pale yellow needles, m. p. and mixed m. p. 302° (decomp.), in very low yield. This material had the same R_F value on the paper chromatogram as an authentic sample run on the same paper (solvents A, B, and C).

Extraction of Dihydromorin.—(*a*) Sawdust from steamed wood (1009 g., dry wt.) was extracted with ether (Soxhlet) for 16 hr. Evaporation of the extract under reduced pressure gave a solid residue which was extracted with boiling water (charcoal). The mixture was filtered and the filtrate, on cooling, deposited colourless crystals of *dihydromorin* (8·08 g., 0·8%) as the hydrate, m. p. 228° (loses water of crystallisation at 147°). Anhydrous dihydromorin was obtained by recrystallisation from ether–light petroleum (b. p. 40—60°) as clusters of needles, m. p. 228°, $[\alpha]_D^{20}$ ±0° (*c* 1·0 in 1 : 1 Me_2CO–H_2O) (Found: C, 59·0; H, 4·0. $C_{15}H_{12}O_7$ requires C, 59·2; H, 3·95%). It was soluble in acetone, ethanol, methanol, ether, and aqueous sodium hydroxide, sodium carbonate, and sodium hydrogen carbonate, and insoluble or only very slightly soluble in light petroleum and in benzene. It gave a red-brown ferric colour in ethanol, a red colour with both magnesium–hydrochloric acid and zinc–hydrochloric acid,[1] and a negative boric acid test.[16] On the paper chromatogram it had R_F 0·60 (solvent A), 0·92 (solvent B), 0·68 (solvent C). Morin on the same paper had R_F 0·25, 0·95, and 0·37 respectively. When the compound was applied to the chromatogram in aqueous solution, and especially with heat, two spots were obtained in solvents A and C owing to the formation of morin by aerial oxidation.

(*b*) Unsteamed wood (51·5 g.) was extracted with ether as above. Evaporation yielded a solid residue (0·58 g.) in which no morin could be detected on the chromatogram, though dihydromorin was shown to be present. Recrystallisation yielded dihydromorin (0·22 g., 0·43%), m. p. and mixed m. p. 224°, R_F as above, $[\alpha]_D^{20}$ ±0° (*c* 0·6 in 1 : 1 Me_2CO–H_2O).

Oxidation of Dihydromorin.—Dihydromorin (1·25 g.) was dissolved in hot water (65 c.c.) in

[11] Wise and Jahn, "Wood Chemistry," Reinhold Publ. Corp., New York, 1952, Vol. I, p. 628 *et seq.*; Barnes and Gerber, *J. Amer. Chem. Soc.*, 1955, **77**, 3259; Suzushino, *Misc. Reports Res. Inst. Nat. Resources (Japan)*, 1954, No. 34, 21; *Chem. Abs.*, 1957, **51**, 1396.

[12] Gage, Douglass, and Wender, *Analyt. Chem.*, 1951, **23**, 1582.

[13] Swain, *Biochem. J.*, 1953, **53**, 200.

[14] Perkin and Everest, "The Natural Organic Colouring Matters," Longmans, Green and Co., London, 1918, p. 213.

[15] Hough, Jones, and Wadman, *J.*, 1949, 2511.

[16] Wilson, *J. Amer. Chem. Soc.*, 1939, **61**, 2303.

an open flask and the solution was heated on a steam-bath with frequent shaking, water being added periodically to replace that lost by evaporation. At 8-hourly intervals, the morin which separated was removed by filtration. The total yield, after 40 hours' heating, was 50%, and the m. p. after recrystallisation from 33% acetic acid was 298° (mixed m. p. 302°) (Found: C, 59·7; H, 3·4. Calc. for $C_{15}H_{10}O_7$: C, 59·6; H, 3·3%). This showed the same R_F value on the paper chromatogram as authentic morin (solvents A and C).

The product (0·28 g.) was methylated with methyl sulphate in acetone,[17] to give penta-*O*-methylmorin, m. p. and mixed m. p. 157—158° (Found: OMe, 39·8. Calc. for $C_{20}H_{20}O_7$: OMe, 41·7%).

The ultraviolet absorption spectra of the morin and penta-*O*-methylmorin prepared in this manner (Fig. 2) corresponded closely to those of authentic samples.

Acetylation of Dihydromorin.—Dihydromorin (0·2 g.) with acetic anhydride (2 c.c.) in pyridine (10 c.c.) gave *penta*-O-*acetyldihydromorin* (0·14 g. after two recrystallisations from methanol), as white needles, m. p. 190—193°, $[\alpha]_D^{20}$ ±0° (*c* 1·0 in Me_2CO) (Found: C, 58·3; H, 4·5; Ac, 39·5. $C_{25}H_{22}O_{12}$ requires C, 58·35; H, 4·3; Ac, 41·8%).

Methylation with Diazomethane.—Dihydromorin in ether was treated with excess of ethereal diazomethane at 0° for 3 days. The solid product (Found: OMe, 12·8%) was recrystallised from benzene–light petroleum and had m. p. 173° (decomp.). Paper-chromatography with butanol–ethanol–water (4 : 1 : 5, top layer) and benzene–pyridine–water (100 : 1 : 100, top layer) [18] showed it to be a mixture in which two components (probably mono- and di-*O*-methyl derivatives) predominated.

Dihydro-5 : 7 : 2′ : 4′-*tetra*-O-*methylmorin.*—Dihydromorin (1 g.) in acetone was methylated with methyl sulphate in the presence of anhydrous potassium carbonate,[3] and the product was recrystallised first from aqueous ethanol and then twice from ethanol–light petroleum to give *dihydro*-5 : 7 : 2′ : 4′-*tetra*-O-*methylmorin* (0·57 g.) as white, feathery needles, m. p. 188—190° (Found: C, 63·5; H, 5·75; OMe, 31·1. $C_{19}H_{20}O_7$ requires C, 63·3; H, 5·6; OMe, 34·4%). The compound gave a red colour with zinc and hydrochloric acid [1] and no colour with ferric chloride in ethanol.

Acetylation of this material gave 3-O-*acetyldihydro*-5 : 7 : 2′ : 4′-*tetra*-O-*methylmorin*, white prisms (from methanol), m. p. 168° (Found: C, 62·3; H, 5·2; Ac, 10·4. $C_{21}H_{22}O_8$ requires C, 62·7; H, 5·5; Ac, 10·7%).

Low-temperature Methylation of Dihydromorin.—Dihydromorin (1 g.) was dissolved in acetone (15 c.c.), and methyl sulphate (10 c.c.) and potassium hydroxide (9 g. in 15 c.c. aqueous solution) were added simultaneously during 3½ hr. with constant stirring, under nitrogen, at ≯0°. The mixture was then acidified and the precipitate remethylated as above. The final product was a viscous oil which was washed with water and crystallised from ethanol–light petroleum, to give pale yellow plates of *substance* (H) (0·14 g.), m. p. 117—118° (Found: C, 64·5; H, 6·35; OMe, 45·6. $C_{21}H_{24}O_7$ requires C, 64·9; H, 6·2; OMe, 47·9%). The compound gave no colour with ferric chloride and an orange colour with alcoholic hydrochloric acid. The ultraviolet absorption spectrum is shown in Fig. 2; no shift was obtained with sodium methoxide or aluminium chloride.[19]

2′-*Hydroxy*-2 : 4 : 4′ : 6′-*tetramethoxychalkone.*—2-Hydroxy-4 : 6-dimethoxyacetophenone (1·25 g.) and 2 : 4-dimethoxybenzaldehyde (1·02 g.) were dissolved in ethanol (25 c.c.) and sodium hydroxide (3 g.) in water (6 c.c.) was added. The mixture was left overnight at room temperature, then acidified with hydrochloric acid. The precipitated chalkone was recrystallised from ethanol [yield, 1·6 g., m. p. 150—152° (lit.,[7] 152°)] (Found: C, 65·9; H, 5·9; OMe, 35·8. Calc. for $C_{19}H_{20}O_6$: C, 66·3; H, 5·9; OMe, 36·0%).

3-*Hydroxy*-5 : 7 : 2′ : 4′-*tetramethoxyflavanone.*—The foregoing chalkone (3 g.) was suspended with shaking in 5% aqueous sodium hydroxide (450 c.c.), and 100-vol. hydrogen peroxide (25 c.c.) added. The mixture was left overnight at 0°. Unchanged chalkone and, presumably, any aurone formed [6] were filtered off, the filtrate was acidified, and the precipitated material was collected. The chalkone was re-treated twice as above and the products were combined and recrystallised from dilute acetic acid, washed with ether, and finally recrystallised from ethanol–light petroleum. It (0·053 g.) had m. p. 179°, mixed m. p. with dihydro-5 : 7 : 2′ : 4′-tetra-*O*-methylmorin prepared by direct methylation of dihydromorin, 183—186°. It gave a red

[17] Jain, Seshadri, and Thiruvengadam, *Proc. Indian Acad. Sci.*, 1952, **36**, *A*, 217.
[18] Simpson and Garden, *J.*, 1952, 4638.
[19] Harborne, *Chem. and Ind.*, 1954, 1142; Swain, *ibid.*, p. 1480.

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colour with zinc and hydrochloric acid, and a green colour with ferric chloride in ethanol, indicating the presence of some tetra-*O*-methylmorin (Found: C, 63·2; H, 5·3; OMe, 34·1. Calc. for $C_{19}H_{20}O_7$: C, 63·3; H, 5·6; OMe, 34·4%).

Attempts to prepare a crystalline acetate were unsuccessful.

Other Experiments.—Attempts to prepare 2 : 2′ : 4-trihydroxy-4′ : 6′-dimethoxychalkone from 2-hydroxy-4 : 6-dimethoxyacetophenone and 2 : 4-dihydroxybenzaldehyde by the above method or by heating the mixture under nitrogen [20] were unsuccessful.

Attempted synthesis of the dihydrotetramethoxyflavonol *via* the corresponding *o*-acetoxychalkone dibromide [21] was unsuccessful.

Suspension of the 2′-hydroxy-2 : 4 : 4′ : 6′-tetramethoxychalkone in alcohol followed by alkaline oxidation [21] furnished some dihydrotetramethoxyflavonol (positive zinc–hydrochloric acid test), but the yield was very small and the product could not be purified.

Attempted Reduction of Datiscetin.—The datiscetin used had m. p. 277° and R_F 0·42 (solvent A), 0·96 (solvent B), 0·30 (solvent C). R_F values for morin, run on the same papers, were 0·30, 0·94, and 0·22 respectively. Reduction of this material (0·2 g.) with dithionite failed to give any appreciable quantity of the dihydro-derivative, while a parallel reduction of quercetin gave dihydroquercetin in good yield.

This work forms part of the current research programme of the Forest Products Research Board, and is published by permission of the Department of Scientific and Industrial Research. The authors thank Professor T. S. Wheeler and Dr. T. Swain for helpful discussion, and Dr. T. H. Simpson for a gift of datiscetin.

Section of Chemistry, Forest Products Research Laboratory,
Princes Risborough, Aylesbury, Bucks. [*Received, May 8th,* 1957.]

[20] Guider, Simpson, and Thomas, *J.*, 1955, 170.
[21] Marathey, *J. Univ. Poona, Science and Technology*, 1953, **4**, 73.

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896. *The Glucomannans from Sitka Spruce* (Picea sitchensis).

By G. O. Aspinall, R. A. Laidlaw, and R. B. Rashbrook.

Hemicellulose fractions composed of D-mannose and D-glucose residues have been isolated from Sitka spruce holocellulose. A methylated glucan and a methylated glucomannan have been prepared therefrom, hydrolysis affording the corresponding 2 : 3 : 6-trimethyl ethers. It is concluded from these and other results that both glucan and glucomannan are linear polysaccharides composed of β-1 : 4-linked sugar residues.

Glucomannans have been isolated from a number of plant sources. The majority of these, for example, the glucomannans from iris seeds [1] and lily bulbs,[2] and the " Iles Mannan " from the tubers of some *Amorphophallus* species,[3,4] appear to function as reserve polysaccharides. All these materials contain essentially linear molecules composed of β-1 : 4-linked sugar residues. Of these polysaccharides, only in the case of " Iles Mannan " has evidence been brought forward to show that glucose and mannose are constituents of the same polysaccharide, rather than arising from a mixture of a glucan and a mannan. It is well known that coniferous woods contain cell-wall polysaccharides giving glucose and mannose on hydrolysis, but little is known concerning the mode or order of linkage of the constituent sugars. Anthis [5] has isolated from the partial hydrolysis of slash pine α-cellulose (containing 10% of mannan) two disaccharides 4-*O*-β-D-glucopyranosyl-α-D-mannose and a mannosylglucose which may be 4-*O*-β-D-mannopyranosyl-α-D-glucose; these disaccharides clearly arise from a glucomannan in the cell-wall structure. It is not

[1] Andrews, Hough, and J. K. N. Jones, *J.*, 1953, 1186.
[2] *Idem*, *J.*, 1956, 181.
[3] Rebers and Smith, *J. Amer. Chem. Soc.*, 1954, **76**, 6097.
[4] Smith and Srivastava, *ibid.*, 1956, **78**, 1404.
[5] Anthis, *Tappi*, 1956, **39**, No. 6, 401.

clear, however, whether such a polysaccharide is a component of the hemicellulose fraction which has resisted extraction by alkali or whether the glucomannan participates in the highly ordered structure of the cellulose. Recently Jones and his collaborators [6] have fractionated the hemicelluloses of Loblolly pine and isolated a glucomannan which also contains a small proportion of D-galactose residues. Here again an essentially linear structure composed of 1 : 4-linked β-D-glucose and β-D-mannose units is indicated. Partial acid hydrolysis of this polysaccharide afforded the following oligosaccharides, 4-*O*-β-D-glucopyranosyl-D-mannose, 4-*O*-β-D-mannopyranosyl-D-mannose, 4-*O*-β-D-mannopyranosyl-D-glucose, and *O*-β-D-mannopyranosyl-(1 ⟶ 4)-*O*-β-D-mannopyranosyl-(1 ⟶ 4)-D-mannose.[7] These results were interpreted as indicating the presence of either a single glucomannan in which glucose and mannose residues are unevenly distributed, or a mixture of a glucomannan and one or more other mannans.

The present paper reports studies carried out on the glucomannans from Sitka spruce (*Picea sitchensis*). Partially delignified sawdust was extracted with cold aqueous alkali to give a complex mixture of polysaccharides yielding glucose, mannose, galactose, xylose, and arabinose on hydrolysis. The residual wood was completely delignified and the resulting holocellulose was extracted with cold 10% sodium hydroxide solution; the hemicellulose fraction after precipitation as the copper complex gave on hydrolysis glucose and mannose in approximately equal amounts. Methylation of the material resulted in the loss of the mannose-containing polysaccharide and a methylated glucan was isolated with an optical rotation indicating a β-linked polymer. Hydrolysis of the methylated polysaccharide gave 2 : 3 : 4 : 6-tetra-*O*-methylglucose (identified by chromatographic mobility and by giving glucose on demethylation), 2 : 3 : 6-tri-*O*-methyl-D-glucose (identified as the crystalline sugar), and some di-*O*-methylhexose (probably arising from incomplete methylation of the polysaccharide). A molecular-weight determination by the isothermal-distillation method (by courtesy of Dr. C. T. Greenwood) gave a value of 8900 ± 500 (degree of polymerisation, 41—46) for the methylated polysaccharide. Although the quantity of non-reducing end-group isolated (1 in 80) was rather less than that required by a linear polymer, it is clear that this methylated polysaccharide is composed of unbranched chains of 1 : 4-linked β-D-glucopyranose residues and is indistinguishable on the present evidence from a methylated degraded cellulose.

The second sample of glucomannan, prepared in a similar manner, contained a higher proportion of mannose residues (mannose : glucose, 2·5 : 1). The consumption of periodate on oxidation was in excess of 1 mole per sugar unit; it is probable, however, that the over-consumption resulted from reactions other than α-glycol scission since the quantity of formic acid released was insufficient to indicate any large proportion of non-reducing end-groups or of 1 : 6-linked hexose units. The quantity of formic acid released during the oxidation was consistent with that from a linear hexosan of *ca.* 45 units. The polysaccharide was converted into a methylated glucomannan, whose optical rotation indicated a β-linked polymer. Hydrolysis of the methylated polysaccharide afforded a tetra-*O*-methylhexose (chromatographically indistinguishable from the 2 : 3 : 4 : 6-tetramethyl ethers of mannose and/or glucose but shown to be mainly the mannose derivative by optical rotation), a mixture of tri-*O*-methylhexoses, and some di-*O*-methylhexoses probably arising from incomplete methylation of the polysaccharide. Separation of the tri-*O*-methylhexoses was effected by selective methyl furanoside formation,[3] and the 2 : 3 : 6-trimethyl ethers of D-mannose and D-glucose were identified as their respective di-*p*-nitrobenzoates. The proportion of 2 : 3 : 6-tri-*O*-methyl-D-mannose to 2 : 3 : 6-tri-*O*-methyl-D-glucose was estimated as 3 : 1 from the optical rotation of the mixture of sugars in water and by the change of optical rotation (undergone solely by the glucose derivative) in methanolic hydrogen chloride. A molecular-weight determination by the isothermal-distillation method gave a value of 10,000 ± 500 (degree of polymerisation, 47—51) for

[6] Ball, J. K. N. Jones, Nicholson, and Painter, *Tappi*, 1956, **39**, No. 6, 438.
[7] J. K. N. Jones and Painter, *J.*, 1957, 669.

the methylated polysaccharide. This value taken together with the quantity of non-reducing end-group (1 in *ca.* 35) indicated that the polysaccharide has an essentially linear structure, although the possibility of a small proportion of molecules containing a single branch point cannot at present be excluded.

Partial acid hydrolysis of the glucomannan was effected by treating the polysaccharide with a mixture of acetic anhydride, acetic acid, and concentrated sulphuric acid at 0° and deacetylating the products with barium methoxide. It has been shown previously [5] that no reversion of monosaccharides occurs under these conditions. A preliminary chromatographic and ionophoretic examination of the products of partial acid hydrolysis showed the presence of glucose, mannose, cellobiose, mannobiose, and a mannosylglucose. The isolation of a mannosylglucose indicates that there is present in the spruce hemicellulose fraction a polysaccharide composed of both mannose and glucose residues.

These results indicate that the glucomannan fraction of Sitka spruce hemicellulose contains at least two essentially linear components, a β-1 : 4-linked glucan and a β-1 : 4-linked glucomannan. On the available evidence we cannot exclude the possibility also of a polysaccharide composed solely of mannose residues. The glucomannan component is clearly similar to the glucomannans previously examined from other plant sources.[1-4] It is increasingly evident from these results and from those of other workers [5-7] that in the coniferous woods there is no clear dividing line on grounds of solubility or of chemical structure between the ordered cellulosic framework, usually of high molecular weight, and the less highly ordered cell-wall polysaccharides or hemicelluloses, usually of lower molecular weight. In the present study it has been shown that polysaccharides composed solely of glucose units, and apparently differing from normal cellulose only in molecular size, may be extracted from the wood, together with glucomannan, by alkali. On the other hand, it is not yet clear whether the mannose units present in some cellulose preparations [5,8] are part of the true cellulose or arise from mannan or glucomannan occluded in the cellulose. It is noteworthy in this respect that the alkaline extraction of synthetic mixtures of ramie cellulose and ivory-nut mannan, prepared by denitration of a mixture of the nitrated polysaccharides, failed to remove all the mannan.[9] Further, evidence for the presence of mannose units in cellulose nitrates of high molecular weight [8] does not adequately prove the presence of mannose units in cellulose since fractional precipitation of mixtures of the nitrates of high-molecular-weight mannose-free ramie cellulose and relatively low-molecular-weight ivory-nut mannan afforded fractions of high molecular weight containing mannose units.[9]

Experimental

Paper chromatography was carried out on Whatman No. 1 filter paper with the following solvent systems (v/v): (A) ethyl acetate–pyridine–water (10 : 4 : 3); (B) butan-1-ol–ethanol–water (4 : 1 : 5, upper layer); (C) benzene–ethanol–water (170 : 50 : 15, upper layer). Paper ionophoresis was carried out in borate buffer at pH 10.[10]

Extraction of Sitka Spruce Glucomannan.—Air-dried sawdust (290 g.), which had been previously extracted under reflux with ethanol–water (85 : 15) and with benzene, was extracted successively with cold and hot water; small quantities of polysaccharide giving on hydrolysis galactose, glucose, and mannose, together with traces of arabinose and xylose, were isolated. Partial removal of lignin was effected by treatment of the residue with sodium chlorite solution acidified by the addition of acetic acid (procedure of Chanda, Hirst, Jones, and Percival [11]), yielding a spruce holocellulose (194 g., dry wt.) (Found: lignin, 5·5%). This material was extracted twice with cold 4% aqueous sodium hydroxide, and neutralisation of the extract with acetic acid followed by the addition of two volumes of ethanol afforded a polysaccharide fraction (9 g.) which gave on hydrolysis glucose, galactose, mannose, arabinose, and xylose.

[8] Timell, *Pulp and Paper Mag. Canada*, 1955, **56**, No. 7, 104.
[9] Snyder and Timell, *Svensk Papperstidn.*, 1955, **58**, 889.
[10] Consden and Stanier, *Nature*, 1952, **169**, 783.
[11] Chanda, Hirst, J. K. N. Jones, and Percival, *J.*, 1950, 1289.

Further extraction of the wood with cold 24% aqueous potassium hydroxide gave a similar complex mixture of hemicelluloses (11 g.). The residual wood was washed with water and delignified again to give a lignin-free residue (105 g., dry wt.). This material was extracted four times with 10% aqueous sodium hydroxide (2 l.) and the extracts were each treated with Fehling's solution (200 ml.). The gelatinous blue precipitates were combined and decomposed with acetic acid, and the resulting solid was washed with 80% acetic acid to remove copper salts and with acetone to remove acid and yielded a white powder. This material was twice precipitated from alkaline solution as the copper complex and regenerated to give glucomannan (sample A; 9 g.). Hydrolysis of the polysaccharide gave glucose and mannose in approximately equal quantities. Sample B, used in all the later experiments, was isolated in a similar manner except that the final reprecipitations *via* the copper complex were omitted. Sample B had $[\alpha]_D^{18}$ −33° (*c* 1·1 in 2N-NaOH) and chromatography of the hydrolysate showed the presence of mannose and glucose in the ratio of 2·5 : 1, together with a trace of xylose.

Methylation of Sample A.—Glucomannan (7·4 g.) was methylated by successive additions of methyl sulphate and sodium hydroxide; neutralisation of the mixture followed by dialysis to remove inorganic salts gave partially methylated polysaccharide (5 g.) (OMe, 38·7%). After a further series of treatments with methyl sulphate and sodium hydroxide the methoxyl content of the methylated polysaccharide (3·5 g.) was raised to 41·6%. A further methylation with methyl iodide and silver oxide failed to raise the methoxyl content of the methylated polysaccharide (3·1 g.) beyond 42% {$[\alpha]_D^{20}$ −9·4° (*c* 3·5 in $CHCl_3$)} {cf. methylated cellulose $[\alpha]_D$ −4° (in $CHCl_3$) [12]}. The methylated glucomannan (1·7 g.) was hydrolysed by formic acid (40 ml.) at 100° for 5 hr.; after removal of formic acid the residual syrup was heated with N-hydrochloric acid (50 ml.) at 100° for 3 hr. After neutralisation with silver carbonate the hydrolysate was concentrated to a syrup (1·6 g.). The mixture of methylated sugars was fractionated on cellulose, with light petroleum (b. p. 100—120°)–butan-1-ol (6 : 4) saturated with water as eluant to give three fractions. Fraction 1 (18 mg.) travelled on the chromatogram at the same rate as 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose and gave glucose on demethylation. Fraction 2 (1·32 g.) crystallised and gave only glucose on demethylation. After two recrystallisations from ether–light petroleum (b. p. 60—80°) the sugar had m. p. and mixed m. p. (with 2 : 3 : 6-tri-*O*-methyl-D-glucose) 115—117°, $[\alpha]_D^{17}$ +100·5° (initial) ⟶ +70·6° (*c* 1·47 in H_2O), and $[\alpha]_D^{17}$ +58·5° ⟶ −36° (28 hr., constant) (*c* 1·49 in methanolic hydrogen chloride). Fraction 3 (93 mg.) contained a mixture of di-*O*-methylhexoses which were not examined further.

Periodate Oxidation of Glucomannan.—Samples of the glucomannan (*ca.* 30 mg.) were shaken in the dark with 0·3M-sodium metaperiodate solution (12 ml.), and determination of the periodate consumed gave the following results (moles consumed per $C_6H_{10}O_5$ residue) : 1·11 (48 hr.); 1·24 (117 hr.); 1·34 (261 hr.).

The glucomannan was oxidised with potassium metaperiodate solution, and the formic acid liberated was determined. The following results were obtained (expressed as the number of $C_6H_{10}O_5$ residues per mole of formic acid liberated); 18·0 (125 hr.); 15·1 (177 hr.); 13·5 (243 hr.); 12·4 (310 hr.). As the formic acid liberated did not reach a constant value, extrapolation to zero time gave a value corresponding to formic acid released from α-glycol scission, namely, 1 mole per 15 $C_6H_{10}O_5$ residues. The release of two mols. of formic acid from the reducing end-group and one mol. from the non-reducing end-group being assumed, this value corresponded to a chain length of 45 residues.

Methylation of Glucomannan.—The glucomannan (sample B) (2·5 g.) was converted into its thallium derivative which was heated with methyl iodide; [13] the product was treated three times in a similar manner and then methylated with silver oxide and methyl iodide, to give a methylated glucomannan (0·77 g.) (Found: OMe, 42·0%), whose methoxyl content could not be raised on further methylation {$[\alpha]_D^{18}$ −13° (*c* 2·48 in $CHCl_3$)}.

The methylated polysaccharide (0·65 g.) was heated with formic acid (20 ml.) in a sealed tube at 100° for 5 hr.; after removal of formic acid the residual syrup was heated with N-hydrochloric acid (25 ml.) at 100° for 3 hr., neutralised with silver carbonate, and concentrated to a syrup (0·54 g.). The mixture of methylated sugars was fractionated on cellulose (53 × 2·1 cm.), with butan-2-one saturated with water as eluant, to give four fractions.

Fraction 1 (15 mg.) had $[\alpha]_D^{18}$ +8° (*c* 1·8 in H_2O) and was chromatographically indistinguishable from the 2 : 3 : 4 : 6-tetramethyl ethers of D-mannose and D-glucose in solvents B and C.

[12] Haworth, Hirst, Owen, Peat, and Averill, *J.*, 1939, 1885.
[13] Fear and Menzies, *J.*, 1926, 937.

Fraction 2 (367 mg.) travelled on the chromatogram at the same rate as 2 : 3 : 6-tri-*O*-methyl-D-mannose and -D-glucose. The optical rotation in water {$[\alpha]_D$ +10·2° (*c* 3·5)} corresponded to that of a mixture of 2 : 3 : 6-tri-*O*-methyl-D-mannose (74%) and 2 : 3 : 6-tri-*O*-methyl-D-glucose (26%). The change in optical rotation in methanolic 1% hydrogen chloride {$[\alpha]_D^{17}$ +22° ⟶ −4° (*c* 0·49)} indicated the presence in the mixture of 25% of 2 : 3 : 6-tri-*O*-methyl-D-glucose. A portion (67 mg.) was dissolved in methanolic 1% hydrogen chloride and kept at room temperature for 20 hr. {$[\alpha]_D^{17}$ +22° ⟶ − 4° (constant)}. After neutralisation with silver carbonate and concentration the derived syrup was fractionated on cellulose (40 × 1·4 cm.) with butan-2-one saturated with water as eluant, to give fraction *a* (23 mg., non-reducing) and fraction *b* (41 mg., reducing). Fraction *a* was hydrolysed by heating with 0·1N-sulphuric acid at 100° for 2 hr., and the resulting reducing syrup (19 mg.) was identified as 2 : 3 : 6-tri-*O*-methyl-D-glucose by conversion into the di-*p*-nitrobenzoate, m. p. and mixed m. p. 187—189·5°. The 2 : 3 : 6-tri-*O*-methyl-D-mannose in fraction *b* was identified by conversion into the di-*p*-nitrobenzoate, m. p. and mixed m. p. (with sample m. p. 187—188°) 181·5—185° (a mixture of the di-*p*-nitrobenzoates of D-glucose and D-mannose trimethyl ethers had m. p. 167—173°). Fractions 3 (92 mg.; R_G 0·55 in solvent B) and 4 (20 mg.; R_G 0·37 in solvent B) contained mixtures of di- and mono-*O*-methyl-sugars which were not examined further.

Acetolysis of Glucomannan and Examination of Derived Oligosaccharides.—The glucomannan (1·0 g.) was dissolved in a mixture of acetic anhydride (12 ml.), acetic acid (12 ml.), and concentrated sulphuric acid (1·2 ml.) at 0° and set aside at room temperature for 120 hr. The mixture was poured into ice-water, neutralised with sodium hydrogen carbonate, and extracted with chloroform, and the extract was dried and concentrated to a syrup (1·0 g.). N-Methanolic barium methoxide (1 ml.) was added to a solution of the sugar acetates in methanol (25 ml.). The mixture was shaken at room temperature for 1 hr. and exactly neutralised with sulphuric acid, and the filtrate was concentrated to a syrup (360 mg.). Chromatography showed the presence of mannose, glucose, traces of galactose and xylose, two disaccharides ($R_{mannose}$ 0·52 and 0·38 in solvent A) and traces of other oligosaccharides. Samples of the two disaccharide components were isolated by fractionation on filter sheets, with solvent A. Component A gave a single spot on the chromatogram ($R_{mannose}$ 0·52) and gave mannose and glucose on hydrolysis, but paper ionophoresis showed two components to be present which had the same mobilities as cellobiose and 4-*O*-β-D-mannopyranosyl-D-mannose. Component B was chromatographically ($R_{mannose}$ 0·38) and ionophoretically identical with 4-*O*-β-D-mannopyranosyl-D-glucose and had $[\alpha]_D^{20}$ +9° (*c* 2·3 in H_2O). Hydrolysis afforded glucose and mannose whereas hydrolysis of the derived glycitol gave only mannose.

The authors thank Professor E. L. Hirst, F.R.S., for his interest and advice, the Department of Scientific and Industrial Research for the award of a Maintenance Allowance (to R. B. R.), and the Rockefeller Foundation and the Earl of Moray Endowment for grants. Some of this work forms part of the programme of the Forest Products Research Board, and we thank the Department of Scientific and Industrial Research for permission to publish these results.

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[*Received, June 6th*, 1957.]

897. *Aromatic Reactivity. Part II.* The Cleavage of Aryltrimethylsilanes by Bromine in Acetic Acid.*

By C. Eaborn and D. E. Webster.

A kinetic study has been made of the reaction between bromine and substituted phenyltrimethylsilanes in acetic acid containing 1·5% of water. This bromodesilylation † reaction, which is an electrophilic aromatic substitution, is of approximately first order in bromine at the concentrations studied (initially, 0·02—0·004M) and is of lower order than the bromination of anisole under similar conditions. Effects of salts and hydrogen bromide are similar to those in aromatic bromination in acetic acid. As in the latter reaction the effective electrophilic reagent is believed to be molecular bromine.

The effects of nuclear substituents on the reactivity of phenyltrimethylsilane form a pattern similar to that in aromatic nitration and protodesilylation,† but somewhat different from that in aromatic molecular halogenation. The reason for this may lie in the availability at the reaction site of the π-electrons of the aryl–Si bond.

Cleavage of Si–aryl bonds by bromine in absence or presence of solvents and of catalysts (usually iron filings) has long been known,[1] and has been used to identify the position of attachment of silicon to a substituted phenyl group,[2] bromine-water then frequently being employed. High yields of products have been obtained from the reaction $Me_3Si{\cdot}C_6H_5 + Br_2 \longrightarrow Me_3SiBr + C_6H_5Br$.[3] Benkeser and Torkelson studied the kinetics of bromine cleavage of some aryltrimethylsilanes in carbon tetrachloride and nitrobenzene and stressed the close similarity between the cleavage and aromatic bromination.[4]

Substituent effects have been reported [5] for acid cleavage of phenyltrimethylsilane (" protodesilylation "), in which the electrophilic reagent is positively charged, and we now describe substituent effects in bromine cleavage (" bromodesilylation ") in acetic acid containing 1·5 wt. % of water, in which, as we shall show, the reagent is molecular bromine. The overall reaction is

$$Me_3Si{\cdot}C_6H_4R + Br_2 \xrightarrow{H_2O} Me_3Si{\cdot}OH + Br{\cdot}C_6H_4R + HBr$$

with the silanol probably condensing rapidly to hexamethyldisiloxane.

Order of Reaction.—Because bromide ion is formed during the bromodesilylation and removes bromine as inactive tribromide ion, the apparent order of reaction rises during a

$$Br_2 + Br^- \rightleftharpoons Br_3^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

run as in aromatic bromination.[6] By comparing times for disappearance of the first 20% of the bromine at various initial concentrations of reactants (cf. ref. 6) the order of the reaction between phenyltrimethylsilane and bromine was found to be between 2·0 and 2·2. By varying the concentrations of each reactant separately the order with respect to each was found to be 1·0 ± 0·1 for bromine concentrations below 0·005M.

We have also measured the value of the equilibrium constant, K, for the equilibrium

* Part I, *J.*, 1956, 4858. † For nomenclature see Part I.

[1] Ladenburg, *Ber.*, 1907, **40**, 2274; Gruttner and Cauer, *Ber.*, 1918, **51**, 1283; Kipping, *J.*, 1921, **119**, 647.

[2] *E.g.*, Kipping and Blackburn, *J.*, 1932, 2200; Kipping and Cusa, *J.*, 1935, 1088; Benkeser and Brumfield, *J. Amer. Chem. Soc.*, 1951, **73**, 4770; Yakubovitch and Motsarev, *J. Gen. Chem. U.S.S.R.*, 1956, **26**, 611.

[3] Pray, Sommer, Goldberg, Kerr, Di Giorgio, and Whitmore, *J. Amer. Chem. Soc.*, 1948, **70**, 433.

[4] Benkeser and Torkelson, *ibid.*, 1954, **76**, 1252.

[5] Eaborn, *J.*, 1956, 4858.

[6] Robertson, *Sci. Prog.*, 1955, **43**, 418.

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(1), and used this to calculate reasonably satisfactory integrated second-order rate constants, k_2, for runs in absence and presence of added bromide ion, using the equation given by Bradfield, Jones, and Orton.[7] Since formation of hydrogen bromide should, by a primary salt effect, lead to a slight increase in k_2 throughout a run, the fall in k_2 found for runs in absence of added bromide at higher bromine concentrations may be real. Since, moreover, the value of k_2 falls somewhat as the initial reactant concentrations are decreased, and since the orders determined by the initial rate method are slightly but consistently greater than 2, it seems that there is a small contribution from a reaction of order higher than second. The values of k_2 for given initial reactant concentrations are higher in presence of added bromide, as expected from operation of a salt effect of a magnitude similar to that observed with lithium chloride.

The order of reaction has not been determined for each of the substituted phenyltrimethylsilanes, but for a pair of compounds examined at the same initial concentrations of reactants the ratio of the times for disappearance of specific fractions of the bromine is approximately constant from 20 to 70% of reaction (with a possible exception noted in the Experimental section), and thus the order of reaction is much the same for both compounds. Since many of the compounds have been directly compared with phenyltrimethylsilane in this way it is likely that the reactions of them all are of approximately first order in bromine for initial bromine concentrations of $<0{\cdot}01$M.

On the other hand, the reaction between bromine and anisole shows a markedly greater fall-off in rate as reaction proceeds. The overall order was found to be *ca.* 2·7 at an initial bromine concentration of *ca.* 0·0025M, which agrees with figures for bromination of aromatic compounds in pure acetic acid at similar bromine concentrations.[6]

The apparent activation energy (*ca.* 12·5 kcal. for phenyltrimethylsilane in the range 25—40°) of the bromodesilylation is similar to that for aromatic brominations at low bromine concentrations.[8]

Salt Effects, and the Nature of the Electrophilic Reagent.—Brominations in pure and aqueous acetic acid have been shown to involve molecular bromine and not positively charged species such as Br^+, $H_2\overset{+}{O}Br$, $H\overset{+}{O}AcBr$.[6,9] Since we use the same arguments to conclude that bromodesilylation also involves molecular bromine we need only outline them. They are: (i) The effect of bromide ion added or formed during a run can be quantitatively accounted for by removal of molecular halogen as tribromide ion. If Br^+ or similar unstable positively-charged entities were involved, the presence of bromide ion would cause a far greater fall in rate.[9] (ii) Acid does not accelerate the reaction, added hydrogen bromide having the same effect as lithium bromide on the rate.

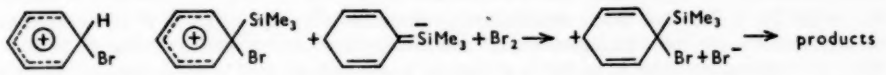
The effects of salts are similar to those in aromatic bromination.[9,10] Salts accelerate in the order $LiClO_4 > LiCl \simeq NaOAc$, the order reflecting the order of dissociation of the salts. Since sodium acetate is a base in acetic acid, the absence of catalysis by it beyond the expected salt effect has been held to indicate in aromatic bromination that detachment of a proton from carbon does not occur in the rate-determining process,[6,10] which is thus formation of the intermediate (I) rather than its destruction.* If this reasoning is accepted, it follows that removal of the trimethylsilyl group is not involved in the rate-determining step of bromodesilylation, which probably then involves formation of the intermediate (II).

However, by analogy with the mechanism suggested for aromatic dedeuteration, sulphonation, and desulphonation,[11] the separation of the proton from complex (I) could

* Hammond (*J. Amer. Chem. Soc.*, 1955, **77**, 334) has pointed out the uncertainty in interpreting kinetic isotope effects, which have also been held to indicate that destruction of (I) is not rate-determining.

[7] Bradfield, Jones, and Orton, *J.*, 1929, 2810.
[8] Robertson, de la Mare, and Johnson, *J.*, 1943, 276.
[9] Robertson, *J.*, 1954, 1267.
[10] (*a*) Robertson, Dixon, Goodwin, McDonald, and Scaife, *J.*, 1949, 294; (*b*) Keefer, Ottenberg, and Andrews, *J. Amer. Chem. Soc.*, 1956, **78**, 255.

be the rate-determining step, but to give a π-complex, a process which would not be base-catalysed, though the subsequent rapid proton loss from this complex would be. Bromodesilylation could similarly involve rate-determining formation of a complex involving interaction of a siliconium ion with the π-electrons of the ring.



(I) (II) (III) (IV)

Substituent Effects.—The relative reactivities of two $R{\cdot}C_6H_4{\cdot}SiMe_3$ compounds can be measured by comparing the times needed for removal of various fractions of the bromine at identical initial concentrations. By overlapping in the pairs, the reactivity, k_{rel}, of each compound relative to phenyltrimethylsilane can be determined, and the results are shown in Table 1 along with the corresponding values, k'_{rel}, observed in protodesilylation.[5]

TABLE 1. *Relative reactivities of* $R{\cdot}C_6H_4{\cdot}SiMe_3$ *compounds.*

R	Bromodesilyln. k_{rel}	Protodesilyln. k'_{rel}	R	Bromodesilyln. k_{rel}	Protodesilyln. k'_{rel}
p-Me	49	21·1	H	1	1
p-Et	45	19·5	*p*-F	0·68	0·75
p-Pr^i	32·5	17·2	*p*-Cl	0·092	0·13
p-Bu^t	29	15·6	*p*-I	0·088	—
m-$Me_3Si{\cdot}CH_2$	9	6·2	*p*-Br	0·071	0·10
p-Me_3Si	3·0(5)	2·5	*m*-Cl	0·003 *	~0·012
m-Me	~2·5	2·3			

* ±0·0002.

In Table 2 the effects of substituents on the reactivity of a single C–H bond of benzene in nitration and molecular halogenation are given for comparison.

TABLE 2. *Partial rate factors in aromatic substitution.*

R [1]	Me	Bu^t	Me_3Si	*m*-Me	H	F	Cl	Br	I	*m*-Cl
Chlorination	870 [2]	—	—	5·0 [2]	1	6·3 [3]	0·4 [3]	0·25 [3]	—	—
Bromination	2420 [4]	780 [5]	—	5·5 [4]	1	4·6 [6]	0·14 [6]	0·06 [6]	0·08 [6]	0·00064 [6]
Nitration [7] ...	54	—	3·1	3·1	1	0·85	0·15	0·10	0·46	0·00106

[1] Substituent *para* unless otherwise indicated. [2] Brown and Stock (*J. Amer. Chem. Soc.*, 1957, **79**, 1421). [3] de la Mare, *J.*, 1954, 4450. [4] Brown and Stock (*loc. cit.*). [5] Calculated from rate factor for *p*-Me [Brown and Stock (*loc. cit.*)] and relative factors for *p*-Me and *p*-Bu^t given by Robertson, de la Mare, and Swedlund (*J.*, 1953, 782). [6] Illuminati and Marino (*J. Amer. Chem. Soc.*, 1956, **78**, 4975). [7] Data listed by Roberts, Sandford, Sixma, Cerfontain, and Zagt (*ibid.*, 1954, **76**, 4525), except for *p*-Me_3Si (Speier, *ibid.*, 1953, **75**, 2930).

The pattern of substituent effects in bromodesilylation differs markedly from that in molecular halogenation, the reaction it might have been expected most to resemble. Halogenation is a much more electron-demanding process as shown by the greater spread of rates and by the greater relative importance of the $+T$ effects of the *para*-halogen atoms which make these much less deactivating relative to the activation by *para*-alkyl groups (*p*-F actually activates). The pattern of substituent effects in bromodesilylation resembles rather closely that in nitration and protodesilylation, and indeed there is quantitative correlation, as shown for the second case by the straight-line log k_{rel}–log k'_{rel} plot in the Figure. As far as comparison may be made, the substituent effects in bromodesilylation also resemble those in bromination by Br^+ or $B\overset{+}{r}OH_2$ [12] (in the latter reaction the rate factors are *p*-Me, 59; *m*-Me, 2·5; *p*-Bu^t, 38·5) and would be wholly consistent with the participation of a positively charged brominating agent as the effective electrophilic

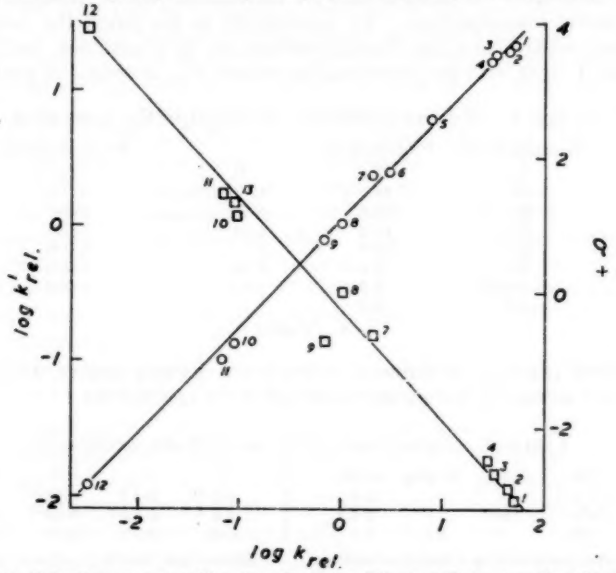
[11] Gold and Satchell, *J.*, 1956, 1635.
[12] de la Mare and Harvey, *J.*, 1957, 131; *J.*, 1956, 36.

entity in bromodesilylation. This possibility seems to be ruled out, however, by the kinetic results discussed above.

Two details of the substituent effects in bromodesilylation are noteworthy. (*a*) Alkyl groups activate in the hyperconjugative order Me > Et > Pr^i > Bu^t, as in protodesilylation, molecular halogenation, and bromination by Br^+ or $BrOH_2^+$ (for the last two only the order Me > Bu^t has been established). Anomalously, the order Bu^t > Me applies in nitration.[13] (*b*) *para*-Halogen atoms deactivate, the rate sequence being F > Cl > Br < I. The same order is found in nitration, halogenation, and brominolysis of phenylboronic acids,[14] and results from opposition of the $-I$ and $+T$ effects of the halogens.

Molecular Bromination and Bromodesilylation.—Because the spread of rates is much

Plot of ○ log k_{rel} (*bromodesilylation*) *against* log k'_{rel} (*protodesilylation*).



□ log k_{rel} *vs.* σ^+. Substituents: 1, *p*-Me; 2, *p*-Et; 3, *p*-Pr^i; 4, *p*-Bu^t; 5, *m*-Me_3SiCH_2; 6, *p*-Me_3Si; 7, *m*-Me; 8, H; 9, *p*-F; 10, *p*-Cl; 11, *p*-Br; 12, *m*-Cl; 13, *p*-I.

greater in molecular halogenation than in nitration, and because conjugative effects of substituents (*e.g.*, of the halogens) are more important in the former process, bromination is regarded as the more electron-demanding process. A review of explanations of this has been given by Berliner and Berliner,[15] whose interpretation we use now. This is that in nitration the entity which enters the ring, *i.e.*, the nitronium ion, is available independently of the aromatic compound, and being highly reactive attacks the nucleus with little assistance from time-variable electromeric effects of the aromatic compound, whereas in bromination the entering entity, Br^+, must be torn from a bromine molecule, with separation of a bromide ion. For this a powerful supply of electrons to the reaction site is necessary, and the electromeric effects of the ring and of conjugated substituents are called fully into play. Furthermore, fission of the bromine molecule has to be assisted by a second electrophilic entity which pulls off bromide ion, *e.g.*, by an additional bromine molecule.

[13] Cohn, Hughes, Jones, and Peeling, *Nature*, 1952, **169**, 291.
[14] Kuivila and Benjamin, *J. Amer. Chem. Soc.*, 1955, **77**, 4834.
[15] Berliner and Berliner, *ibid.*, 1954, **76**, 6179.

It is reasonable to assume that the difference between bromodesilylation and bromination arises from a greater availability of electrons at the reaction site in the former process. This could originate partly in inductive release of electrons from the trimethylsilyl group to the neighbouring ring carbon atom, but because of p_π–d_π bonding between the ring and the silicon atom the overall supply of electrons to the ring is, in fact, very small (and in certain structures the trimethylsilyl group withdraws electrons from the ring).[17] It may be that the availability at the reaction site of the π-electrons of the Si–C bond leads to polarisation of the attacking bromine molecule without large assistance from the time-variable effects of the ring and of substituents, the effect being clearly revealed if, for simplicity, the silicon compound is regarded as reacting in one of its extreme mesomeric forms (III). The electron-availability in the C–Si bond could also lead to fission of the bromine molecule without the need for an additional bromine molecule to pull away bromide ion, and thus to a reaction of lower order than aromatic bromination.

Substituent Constants for Electrophilic Aromatic Substitution.—Brown and Okamoto [16(b)] have recently described a set of substituent constants (σ^+-constants) analogous to Hammett σ-constants [18] but applicable to electrophilic nuclear and side-chain reactions. A plot of log k_{rel} for bromodesilylation against these σ^+-constants is an excellent straight line (see Fig.) and provides further justification for Professor H. C. Brown's approach to substituent effects in aromatic substitution.

While recognising the value of this approach, we would point out that the correlations so obtained should not be allowed to obscure important differences between the reactions. Since the σ^+ constants seem effectively to cover nitration, halogenation, protodesilylation, bromodesilylation, and other reactions,[16(b)] one might conclude that there are no anomalies in the substituent effects, whereas the differences between the pattern of substituent effects in nitration and molecular halogenation, for example, are of considerable significance in considering detailed mechanisms (cf. ref. 15).

Experimental

Materials.—Acetic acid was purified [19] and fractionated, and water was added to give a f. p. of 13·60°. This corresponds with a water content of 1·50 wt. % (confirmed by Karl Fischer titration).

Bromine was distilled from potassium bromide. Hydrogen bromide was prepared from bromine and tetralin and was passed through tetralin bubblers and cold traps into the solvent, the bromide ion content then being determined by titration.

The dried lithium salts gave neutral solutions in water.

Phenyltrimethylsilanes.—Gas–liquid chromatography showed these to contain only traces of impurities, except for *p*-bromophenyltrimethylsilane from which an impurity (<3%) could not be removed. This impurity, probably *p*-di(trimethylsilyl)benzene, caused an initial fast removal of a small amount of bromine in the rate studies.

p-*Iodophenyltrimethylsilane*, prepared in *ca.* 30% yield from iodine and the Grignard reagent from *p*-bromophenyltrimethylsilane and magnesium in ether, had b. p. 155°/50 mm., n_D^{20} 1·5652 (Found: C, 39·3; H, 4·8. $C_9H_{13}ISi$ requires C, 39·1%; H, 4·7%).

Rate Studies.—The bromine solution was standardised and an organosilane solution of appropriate (usually equal) concentration was prepared. Equal volumes of the solutions, both at thermostat temperature (25·00° ± 0·02°), were mixed, the point of half-addition being taken as zero time. Samples removed by automatic pipette were added to aqueous potassium iodide and the liberated iodine was titrated against sodium thiosulphate solution by a potentiometric (dead-stop end-point) technique. Titrations were accurate to 0·005 ml. of 0·005N-thiosulphate.

Loss of bromine by volatilisation or by reaction with the acetic acid was insignificant except for the slowest runs, involving *m*-chlorophenyltrimethylsilane, in which appropriate corrections were made.

[16] (*a*) de la Mare, *J.*, 1954, 4450; (*b*) Brown and Okamoto, *J. Amer. Chem. Soc.*, 1957, **79**, 1913.
[17] Chatt and Williams, *J.*, 1954, 4403; Benkeser and Krysiak, *J. Amer. Chem. Soc.*, 1953, **75**, 2421; Eaborn and Parker, *J.*, 1954, 939.
[18] Jaffé, *Chem. Rev.*, 1953, **53**, 191.
[19] Orton and Bradfield, *J.*, 1927, 983.

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The organosilanes were shown spectrophotometrically [5] not to react with the solvent at a significant rate. Some were cleaved by added hydrogen bromide, but not at a rate which was significant in any of the runs reported.

Runs were initially carried out in blackened vessels but this was later found to be unnesessary.

Determination of Order.—Phenyltrimethylsilane was used, and Table 3 shows the effect on the times, t (in sec.), for removal of 10, 20, and 50% of the bromine of halving the initial (equal) concentrations of both reactants. The order, n, of the reaction calculated from these times is also shown. These runs are only to be used in the pairs shown, as relative rather than absolute accuracy was sought.

TABLE 3.

$10^3 \times$ Concn. (M)	$t_{10\%}$	$t_{20\%}$	$t_{50\%}$	$n_{10\%}$	$n_{20\%}$	$n_{50\%}$
4·45	1150	2975	13,950	2·08	2·07	2·00
8·9	545	1415	7000			
10·13	330	1020	6120	2·09	2·06	2·00
20·25	155	490	3060			
20·95	120	360	2790	~2·12	2·17	1·98
41·9	~55	160	1410			

By varying the concentration of each reactant separately, and taking times to 10% of reaction as proportional to initial rates, the order with respect to each reactant was found to be 1·0 ± 0·1 for <0·005M-bromine.

In the following typical runs (Table 4) the times were taken from smoothed curves, and the integrated rate constants, k_2, calculated from the formula given by Bradfield, Jones, and Orton,[7] or from a special form (kindly derived by Mr. C. A. Haywood) applicable to runs involving equal concentrations of reactants in absence of added bromide, *viz.*,

$$\frac{ktK}{2{\cdot}303} = 2\log\left(\frac{2v_0 + K}{2v + K}\right) - \left(2 - \frac{K}{2a}\right)\log\frac{v_0}{v} - \frac{K(v - v_0)}{2{\cdot}303v_0v} - \left(\frac{K}{2a}\right)\log\left(\frac{v_0 + 2a}{v + 2a}\right)$$

where a, c, and b are the initial concentrations of bromine, organosilane, and added lithium bromide, respectively, and the other symbols are as previously used.[7] The value of K is 0·0055 (see below).

TABLE 4.

(i) $a = 0{\cdot}0125$M. $c = 0{\cdot}0250$M. $b = 0$.

Br_2 used (%)	10	20	30	40	45	50	55	60	70
Time (sec.)	160	370	670	1100	1390	1765	2180	2730	4330
10^2k_2 (sec.$^{-1}$ mole^{-1} l.)	2·8	2·8	2·80	2·75	2·70	2·58	2·57	2·52	2·52

(ii) $a = c = 0{\cdot}003172$M. $b = 0$.

Br_2 used (%)	10	20	30	40	50	65
Time (sec.)	1260	3720	6510	10,560	16,380	32,700
10^2k_2 (sec.$^{-1}$ mole^{-1} l.)	2·17	2·21	2·21	2·18	2·17	2·15

(iii) $a = 0{\cdot}0125$M. $c = 0{\cdot}025$M. $b = 0{\cdot}050$M.

Br_2 used (%)	10	20	30	40	45	50	60	65
Time (sec.)	1290	2880	4950	7500	9030	10,830	15,600	18,600
10^2k_2 (sec.$^{-1}$ mole^{-1} l.)	2·86	2·82	2·81	2·80	2·80	2·78	2·78	2·78

(iv) $a = 0{\cdot}0125$M. $c = 0{\cdot}025$M. $b = 0{\cdot}10$M.

Br_2 used (%)	10	20	30	40	45	55	60
Time (sec.)	2130	4860	7980	12,210	14,970	21,060	24,960
10^2k_2 (sec.$^{-1}$ mole^{-1} l.)	3·38	3·32	3·23	3·37	3·33	3·32	3·23

Runs involving added hydrogen bromide were identical within experimental error with those involving lithium bromide.

In the reaction between anisole (0·0033M) and bromine (0·0033M), 10 and 20% of the bromine was used up in ~80 and 240 sec., respectively. With both anisole and bromine initially 0·00165M, the corresponding times were 275 and 800 sec. These figures correspond with an order of 2·8 and 2·7 based on 10 and 20% of reaction, respectively.

Salt Effects.—Table 5 shows the effects of salts on the reaction between phenyltrimethylsilane (initially 0·025M) and bromine (initially 0·0125M). The time for removal of half of the bromine is given in each case along with the " relative rate," which is the average ratio of the times for removal of specific fractions (20—70%) of the bromine in absence and in presence of salts. Variations of this ratio from the average during a run were small (<±2%) and random.

TABLE 5.

Salt	—	$LiClO_4$	$LiClO_4$	$LiClO_4$	LiCl	LiCl	LiCl	NaOAc	NaOAc	NaOAc
10^2Salt (M)	—	2·50	5·0	10·0	2·50	5·0	10·0	2·50	5·0	10·0
$t_{\frac{1}{2}}$ (sec.)	1760	1485	1285	990	1600	1560	1450	1560	1495	1440
Rel. rates ...	1	1·17	1·36	1·76	1·08	1·13	1·24	1·15	1·19	1·24

Table 6 shows the effect of added hydrogen bromide on the instantaneous rate, $v_{30\%}$, of the reaction between phenyltrimethylsilane (0·025M) and bromine (0·0125M) after removal of 30% of the bromine (the rates being given by the slopes of the time–titre curves). The ratios of the rates in presence and absence of added hydrogen bromide are shown. The concentrations, $[Br_2]_{30\%}$, of free bromine at 30% reaction (calculated by using 0·0055 as the value of K) are also given, along with the ratio of these concentrations in presence and in absence of added bromide. The two ratios are in reasonable agreement, the rate ratio rising slightly relative to

TABLE 6.

[HBr] (added) (M)	0	0·0125	0·0250	0·050	0·100
$10^7 v_{30\%}$ (mole sec.$^{-1}$)	4·03	1·89	1·09	0·66	0·37
Rel. rate	1	0·47	0·27	0·16	0·09
$10^3[Br_2]_{30\%}$ (free) (M)	6·69	3·01	1·76	0·94	0·48
Rel. free Br_2 concn.	1	0·45	0·26	0·14	0·07

the free-bromine ratio as the amount of added hydrogen bromide is increased, as expected from the operation of a salt effect similar to that of lithium chloride.

Reaction Rates.—For each substituted phenyltrimethylsilane, R·C_6H_4·$SiMe_3$, the following list shows the half-life of one reaction involving equal initial concentrations of silane and bromine. The substituent, R (*para* unless otherwise specified) is given along with 10^3 × initial concn. of both reactants (M) and the half-life time in sec: Me, 2·495, 431; Bu^t, 4·10, 540; Pr^i, 4·10, 490; Et, 4·10, 345; Me_3Si, 8·80, 2100; *m*-Me_3Si·CH_2, 13·1, 492; F, 25·3, 3540; Cl, 25·4. 28,200; I, 15·31, 33,500; Br, 32·5, 26,820; *m*-Cl, 78·2, 219,600.

Relative Reactivities.—Solutions of two organosilanes were prepared to be of exactly the same concentration as a standardised bromine solution. The times for disappearance of specific fractions of the bromine were compared directly, usually for 20—70% of reaction. The typical comparison (Table 7) refers to *p*-trimethylsilylphenyl- and phenyl-trimethylsilane ([Silane] = $[Br_2]$ = 0·0135M).

TABLE 7.

Reaction (%)	20	30	40	50	60	70
Time (sec.) (R = H)	715	1410	2430	4110	7020	13,500
Time (sec.) (R = *p*-Me_3Si)	235	460	800	1350	2305	4440
10^3 × Rel. rate	304	306	304	304	305	304

Table 1 is based mainly on the following direct comparisons. For each pair of R·C_6H_4·$SiMe_3$ compounds (substituents *para* unless otherwise indicated) the average inverse ratio of times for disappearance of specific fractions of bromine is given along with the limits of variation in the ratio during 20—70% of reaction: Me/H, 48·8 ± 0·5; Pr^i/Bu^t, 1·12 ± 0·03; Me/Et, 1·07(5) ± 0·01(5); Et/Bu^t, 1·54 ± 0·02; Pr^i/*m*-Me, 13·1 ± 0·3; Pr^i/H, 32·5 ± 0·3; *m*-Me_3Si·CH_2/H, 9·1 ± 0·5; Me_3Si/H, 3·05 ± 0·01; H/F, 1·47 ± 0·04; F/Cl, 7·3 ± 0·2; Cl/Br, 1·29 ± 0·03; I/Br, 1·26(5) ± 0·01(5); H/I, 11·3 ± 0·1; Cl/I, 1·04 ± 0·01; Cl/*m*-Cl, 31 ± 2.

(For the *m*-Me/H pair the ratio varied more seriously. Because of this effect, which is being investigated, only an approximate reactivity is given for the *m*-Me compound in Table 1.)

Equilibrium Constant for Formation of Tribromide Ion.—The equilibrium constant, K (*i.e.*, $[Br^-][Br_2]/[Br_3^-]$), was determined by the spectrophotometric method,[10(b),20] a series of solutions containing lithium bromide (0·004—0·02M) and bromine (6×10^{-5}—3×10^{-4}M) in 98·5% acetic acid being used. Optical densities were determined at 340, 350, and 360 mμ in 1 cm. cells at 25·00° ± 0·02° against a solvent blank. Table 8 shows the values of K determined, along with the molar extinction coefficient of tribromide ion and of bromine ($\varepsilon_{Br_3^-}$ and ε_{Br_2} respectively) at each wavelength.

[20] Ketelaar, van der Stolpe, Goudsmit, and Dzcubas, *Rec. Trav. chim.*, 1952, **71**, 1104.

TABLE 8.

λ(mμ)	ε_{Br_2}	$\varepsilon_{Br_2^-}$	K	λ(mμ)	ε_{Br_2}	$\varepsilon_{Br_2^-}$	K	λ(mμ)	ε_{Br_2}	$\varepsilon_{Br_2^-}$	K
340	42	2340	0·0055	350	68	1460	0·0056	360	100	1050	0·0057

We thank the Department of Scientific and Industrial Research for a maintenance grant to one of us (D. E. W.), and Imperial Chemical Industries Ltd. for a grant towards the cost of chemicals.

THE UNIVERSITY, LEICESTER. [*Received, June 4th*, 1957.]

898. *Exchange Studies of Certain Chelate Compounds of the Transitional Metals. Part III.* Exchange and Electron-transfer Reactions involving Phenanthroline and Dipyridyl Complexes of Cobalt*(III).

By PETER ELLIS, R. G. WILKINS, and M. J. G. WILLIAMS.

The tris-(1 : 10-phenanthroline)- and tris-(2 : 2′-dipyridyl)-cobalt(III) ions are inert to exchange with the corresponding free ligands in acid solution. They undergo exchange in neutral solution however owing, almost certainly, to catalysis by cobalt(II) impurity, present in small amounts in different samples of the cobalt(III) complexes. The addition of a small amount of cerium(IV) to the $[Co\ dipy_3]^{3+}$ ion suppresses exchange in neutral solution. By studying the effect of added cobalt(II) on the exchange rate the amounts of impurity in each complex can be assessed. The values obtained agree well with those from magnetic measurements. It is also possible to assign approximate (assumed) second-order rate constants to the two fast electron-transfer processes, involving cobalt(II) and cobalt(III) complexes with these ligands, and the results are briefly discussed. The importance of traces of impurities in exchange studies, already emphasised by previous investigators, is reiterated.

IT has been reported that, although tris-(1 : 10-phenanthroline)cobalt(III) chloride, $[Co\ phen_3]Cl_3$, gives a red colour with ferrous sulphate solution only on long boiling, one phenanthroline molecule can be easily removed by refluxing a suspension of the chloride in chloroform to form $[Co\ phen_2Cl_2]Cl$.[1] It is surprising that change of solvent should have such a drastic effect on the ease of dissociation of the complex and some doubt exists as to the " lability " of the complex, so that a statement such as " one molecule of the base is easily disengaged and replaced by aquo-groups," reasonable in view of the known facts about the compound, appears in the literature.[2]

The rates of substitution of cobalt(III) complexes are usually slow,[3] as, for example, in the slow exchanges that have been observed with such complexes.[4] About the only exception to this generalisation is the rapid $H_2{}^{18}O$ exchange with the $Co_{aq.}{}^{3+}$ ion. Since with the conditions of this experiment the $Co_{aq.}{}^{3+}$ ion contained substantial amounts of the $Co_{aq.}{}^{2+}$ ion, the known rapid Co(II)–Co(III) electron transfer plus the lability of the $Co_{aq.}{}^{2+}$ species forms an effective path for the apparent rapid exchange [5] of $Co_{aq.}{}^{3+}$. In continuation of our exchange studies [6] with [^{14}C]phenanthroline and [^{14}C]dipyridyl we have investigated the behaviour of the phenanthroline- and the dipyridyl-cobalt(III) complex in an attempt to resolve the problem of the lability of these ions.

* Part II, *J.*, 1957, 1763.

[1] Pfeiffer and Werdelmann, *Z. anorg. Chem.*, 1950, **263**, 31.
[2] Brandt, Dwyer, and Gyarfas, *Chem. Rev.*, 1954, **54**, 959.
[3] Taube, *Chem. Rev.*, 1952, **50**, 69.
[4] Stranks and Wilkins, *Chem. Rev.*, in the press.
[5] Hunt and Taube, *J. Chem. Phys.*, 1951, **19**, 602.
[6] Wilkins and Williams, *J.*, 1957, 1763.

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Experimental

Materials.—[^{14}C]Phenanthroline hydrate and [^{14}C]dipyridyl were prepared as described previously.[7] Various samples of the cobalt(III) complexes, $[CoA_3](ClO_4)_3,xH_2O$, were prepared as described below. "A" signifies either dipyridyl ($x = 3$; prefaced D) or phenanthroline ($x = 2$; prefaced P). Each sample was recrystallised at least twice from hot water.

Samples D1, D2, D4, and P4 were prepared by oxidation of the cobaltous complex with hydrogen peroxide.[8] The visible spectra of a 3·9 mmolar solution of D1 had $\varepsilon_{max.}$ 75·1 at 4460 Å (Yamasaki [9] reports a maximum at 4500 Å).

Several samples were prepared by refluxing the *purpureo*-chloride, $[Co(NH_3)_5Cl]Cl_2$ (0·4 g.), with dipyridyl or phenanthroline (0·6 g.) in 30% methanol (30 c.c.) until ammonia was no longer evolved.[1] Sample P1 separated (as the chloride) on concentration of the final solution; [1] samples D3 and P2 were precipitated by addition of sodium perchlorate to the refluxed solution.

Specimen P3 was prepared and isolated like P2 except that aquopenta-amminocobalt(III) nitrate was the starting material. The reaction was much slower than with the *purpureo*-chloride and was left for 40 hr. for completion. Sample D5 was obtained by recrystallising D4 from solutions containing cerium(IV). P5 was one of the products from the reaction between $[Co\ en_2(Cl)(H_2O)]SO_4$ and phenanthroline.[10] $[Co\ phen_3]^{3+}$ ion remains in the mother-liquor after removal of $[Co\ en_2\ phen]Cl(SO_4)$ and may be precipitated from it as the perchlorate.

These samples were analytically pure. Representative analyses follow: D1 (Found: C, 40·3; H, 3·4; N, 9·6. Calc. for $C_{30}H_{24}O_{12}N_6Cl_3Co,3H_2O$: C, 41·1; H, 3·5; N, 9·5%); P2 (Found: C, 45·3; H, 3·2; N, 8·9. Calc. for $C_{36}H_{24}O_{12}N_6Cl_3Co,2H_2O$: C, 45·3; H, 3·15; N, 8·9%).

Tris-(*o*-phenanthroline)cobalt(II) perchlorate monohydrate was prepared for magnetic measurements [11] (Found: C, 53·0; H, 3·3; N, 10·3. Calc. for $C_{36}H_{24}O_8N_6Cl_2Co,H_2O$: C, 52·9; H, 3·2; N, 10·3%).

Exchange Experiments.—Most of the runs described were performed at about neutral pH. The complex perchlorate was mixed with inactive base (phenanthroline or dipyridyl) and equilibrated at the required temperature. A small amount of radioactive base dissolved in water was added (zero time) and separation effected, at various times, by extracting the base with benzene, and, after concentration, precipitating the complex as perchlorate. The complex was counted as the perchlorate by methods already described.[12] In the experiments in acid solution a different method was required since perchlorate does not precipitate the complex or the base; as the latter is present as protonated species it is not extracted appreciably from aqueous solution. The exchange mixture after being cooled to 0° was treated with chloropalladite in 2N-hydrochloric acid (after adding inactive base as carrier if necessary to give sufficient material for radioassay). The brown precipitate was left for a few minutes, centrifuged, and washed with water. It was then heated in boiling water, whereupon the cream-coloured $[Pd\ phenCl_2]$ [13] was obtained and was washed with ethanol, then ether, and dried at 105° (Found: C, 40·0; H, 2·2; N, 8·0. Calc. for $C_{12}H_8N_2Cl_2Pd$: C, 40·5; H, 2·2; N, 7·85%). The specific activity of the base before being mixed with cobalt(III) complex, directly after being mixed, and after being refluxed for some hours was measured (in the form of the palladium complex) and the similar values for each condition indicated that (*a*) no phenanthroline was removed from the complex by acid, and (*b*) no exchange occurred under these conditions.

Cobalt(II) *Catalysed Experiments.**—By observing the variation of the rate of exchange, which always followed a first-order law, with the concentration of added cobalt(II) salt, the concentration of cobalt(III) complex and of added base being kept constant, it was possible to estimate the amount of cobalt(II) impurity (x) in the original cobalt(III) sample, and the approximate second-order rate constant (k_2) for the electron-transfer process. The assumption was made that the electron-transfer process was of second order (reasonable in

* In this section brackets are not used to enclose the formula of a complex ion; they are here used for the customary designation of molar concentration.

[7] Ellis, Wilkins, and Williams, *J.*, 1956, 3975.
[8] Nyholm and Burstall, *J.*, 1952, 3570.
[9] Yumasaki, *Bull. Chem. Soc.* (*Japan*), 1937, **12**, 390.
[10] Jaeger, *Z. anorg. Chem.*, 1928, **170**, 384.
[11] Pfeiffer and Werdelmann, *ibid.*, 1950, **261**, 197.
[12] Popplewell and Wilkins, *J.*, 1955, 4098.
[13] Ryan, *Canad. J. Res.*, 1949, **27***B*, 938.

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view of the number of known electron transfers which obey this rate dependence [14]) and also that the direct exchange of CoA_3^{3+} was extremely slow (k_1 very small) in neutral solution. With the cobalt(III) complex alone

$$R = \frac{0{\cdot}693}{t_{\frac{1}{2}}} \cdot \frac{3[CoA_3^{3+}][A]}{3[CoA_3^{3+}] + [A]} = k_1[CoA_3^{3+}] + k_2[CoA_3^{3+}]x$$
$$\simeq k_2[CoA_3^{3+}]x$$

and with added y-molar Co^{2+} ion

$$R' = \frac{0{\cdot}693}{t_{\frac{1}{2}}} \cdot \frac{3[CoA_3^{3+}][A]}{3[CoA_3^{3+}] + [A]} \simeq k_2[CoA_3^{3+}](x + y)$$

so that $k_2\{= (R' - R)/[CoA_3^{3+}]y\}$ and x were easily obtained.

In these experiments it was considered that there was a sufficient concentration of ligand A to form a complex CoA_3^{2+} with all the cobalt(II) ion present so that it was not necessary to consider electron-transfer processes involving CoA_2^{2+}, etc. A solution of the cobalt(III) complex was prepared and similar amounts were used in all the catalysed experiments in order to duplicate as far as possible the amounts of impurity in each run. A small zero-time exchange occurred in the experiments catalysed by cobalt(II); this arose since the small amount of cobalt(II) complex, which attains an appreciable activity rapidly, follows the cobalt(III) complex in the separation procedure. The results of the exchange work are given in Table 1. The run numbers are given for designation purposes only. Work not recorded in the Table ruled out the possibility of photocatalysed exchange.

TABLE 1. *Exchange of* $[Co\ phen_3]^{3+}$ *with phenanthroline and* $[Co\ dipy_3]^{3+}$ *with dipyridyl under various conditions.*

Run No.	Sample	Species present	Temp.	[Complex] (mmole l.$^{-1}$)	[Base] (mmole l.$^{-1}$)	$t_{\frac{1}{2}}$ (exch.) (min.)	10^5R (min.$^{-1}$ mole l.$^{-1}$)
1	D1	—	45·2°	4·0	21·6	210	2·6
2	D1	—	45·2	3·9	12·4	150	2·8
3	D2	—	45·0	3·9	12·5	150	2·8
4	D3	—	45·0	3·9	12·4	206	2·0
5	D4	—	45·0	3·9	12·3	174	2·40
6	D4	15μM-Co(II)	45·0	3·9	12·3	47	8·84
7	D4	31μM-Co(II)	45·0	3·9	12·2	26	15·9
8	D4	2·1mM-$S_2O_8^{2-}$	45·0	4·2	10·3	complete exch. in 24 hr.	
9	D4	1·8mM-Ce(IV)	45·0	4·2	10·3	no exch. in 24 hr.	
10	D5	—	45·0	4·2	10·3	complete exch. in 20 hr.	
11	D4	2M-HCl	reflux	4·0	0·08	no exch. in 15 hr.	
12	P1	—	0·0	1·0	10·0	complete exch. in 5 min.	
13	P2	—	34·9	1·6	9·1	298	0·7
14	P3	—	45·0	1·3	9·4	26	7·3
15	P3	—	20·0	1·2	5·65	76	2·0
16	P3	31μM-Co(II)	20·0	1·2	5·77	50	3·06
17	P3	45μM-Co(II)	20·0	1·2	5·66	44	3·46
18	P3	O_2 through soln. 12 hr.	45·0	1·15	3·5	415	0·3
19	P4	—	17·0	1·6	10·0	45	5·0
20	P3	2M-HCl	reflux	4·0	0·08	no exch. in 17 hr.	

Attempted Resolutions.—Several attempts were made to resolve $[Co\ phen_3](ClO_4)_3$, tartrate, antimonyl tartrate, and α-bromocamphor π-sulphonic acid being used as resolving agents. Because of the very high solubility of most $[Co\ phen_3]^{3+}$ salts, extensive evaporation was necessary to isolate solids, none of which showed any optical rotation (sodium light). The ion should be resolvable, but working in acid solution may be a distinct advantage in view of its exchange (and possible racemisation) behaviour in neutral solution. It is perhaps significant that no direct resolution of a tervalent metal complex of phenanthroline or dipyridyl has been reported; rather the desired optical isomers have been obtained by oxidation of the corresponding optically-active bivalent metal complex.[2]

[14] (*a*) Amphlett, *Quart. Rev.*, 1954, **8**, 219; (*b*) Zwolinski, Marcus, and Eyring, *Chem. Rev.*, 1955, **55**, 157.

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Acid Dissociations.—These experiments were carried out by dissolving the complex perchlorate (40 mg.) in 5N-sulphuric acid (20 ml.). One portion was refluxed for 3 hr. and the other kept in ice-water. Within experimental error no difference in optical density between the two solutions was observed, indicating that no slow dissociation of the complex occurred.

Magnetic Measurements.—We are grateful to Dr. J. Lewis and Mr. A. Earnshaw for assistance with these measurements. The Gouy method, involving the normal arrangements, was used and measurements on the cobalt-(II) and -(III) compounds were carried out at room temp. (19°) and at liquid-nitrogen temperature. The absence of ferromagnetic impurities was indicated by the lack of variation of susceptibility with field strengths from about 6000 to 10,000 gauss.

If the mole-fractions of cobalt-(III) and -(II) complexes present in the impure samples of the cobalt(III) complexes are represented by x_3 and x_2, and their molar magnetic susceptibilities by ψ_3 (which should be independent of temperature) and ψ_2 at 292° and ψ_2' at 78° K, and the observed molar susceptibilities of the impure cobalt(III) sample are signified by ψ_{292} and ψ_{78} then

$$\psi_{292} = \psi_3 x_3 + \psi_2 x_2$$

$$\psi_{78} = \psi_3 x_3 + \psi_2' x_2$$

and

$$x_2 = (\psi_{78} + \psi_{292})/(\psi_2' - \psi_2)$$

The results are given in Table 2. The values of ψ_2 for $[Co\ dipy_3](ClO_4)_2$ at 292° and 78° K were assumed to be the same as for the analogous phenanthroline compound. The value of 96·6 was reported [8] for the former at room temperature so that the assumption is reasonable. The

TABLE 2. *Magnetic measurements of cobalt*(II) *and cobalt*(III) *phenanthroline and dipyridyl complexes.*

Compound	Temp. (° K)	$10^4\psi$	x_2	Temp. (° K)	$10^4\psi$
$[Co\ phen_3](ClO_4)_3$ (P3)	292	1·16	0·033	78	9·20
$[Co\ phen_3](ClO_4)_3$	292	108		78	352
$[Co\ dipy_3](ClO_4)_3$ (D1)	292	−1·74	0·018	78	2·69

estimation of the purity of the cobalt(III) dipyridyl complex was carried out on sample D1 although sample D4 was used for the kinetic method [*i.e.*, by adding cobalt(II)]. There was very little difference between these samples. There appeared to be a definite relation between the value of ψ_{292} and the kinetic rate (the lower the value of ψ_{292} the lower the rate). A value of 5·2 B.M. was obtained for the magnetic moment of $[Co\ phen_3](ClO_4)_2,H_2O$ from these measurements with a molecular field constant θ of 17°.

RESULTS and DISCUSSION

An apparently pure sample of $[Co\ dipy_3](ClO_4)_3$ (D1) underwent exchange at a measurable rate in neutral solution (runs 1 and 2 are typical of several runs carried out with this material) and further recrystallisations did not alter this rate (D2, run 3). Exchange experiments with $[Co\ phen_3]^{3+}$ indicated that this ion was extremely labile (P1, run 12). It became apparent that samples of $[Co\ phen_3](ClO_4)_3,2H_2O$ further purified by recrystallisation or prepared by different methods gave slower and differing rates of exchange in neutral solution (P2, P3, and P4, runs 13—15 and 19). Also a sample aerated for 12 hours gave markedly lower exchange rates (P3, run 18). These results redirected our attention to the dipyridyl work and the exchange of a new sample of $[Co\ dipy_3](ClO_4)_3,3H_2O$, prepared from cobalt *purpureo*-chloride (D3, run 4) indicated that with this compound, too, erratic rates could be obtained although the effect was much less marked than with the phenanthroline compounds.

Experiments in acid solution proved helpful. Neither complex lost colour even after 3 hours at 80—100° and did not undergo exchange after 15 hours' refluxing in 2M-hydrochloric acid (runs 11 and 20). These results were independent of the nature of the sample. Since the acid and base forms of the ligands attain equilibrium rapidly, this reduced rate cannot arise from the presence of very small amounts of the free base forms in these acid conditions. Exchange studies have shown that the rates of dissociation of nickel, cobalt(II),

and iron(II) phenanthroline complexes are independent of pH and those of nickel and iron(II) dipyridyl complexes faster in acid; [6,16] so the results in acid strongly indicated that dissociation of the cobalt(III) complexes in neutral solution also was extremely slow and that the observed exchange arose from the presence of a catalyst, probably small amounts of cobalt(II) present as the aquated or complexed ion. With the condition of ligand exchange, the cobalt impurity will exist mainly as $[CoA_3]^{2+}$ in neutral solution but will be completely dissociated in strongly acid solution. This explanation is reasonable since it was shown in other exchange experiments (runs 6, 7, 16, and 17) in which small amounts of cobalt(II) ion were deliberately added, that a marked enhancement of exchange rate occurred. The results of runs 5—7 and 15—17 being used, the percentage of cobalt(II) impurity in samples D4 and P3 was estimated to be 1·4 and 5·4%, respectively. These results agreed reasonably with values from magnetic measurements (1·8 and 3·3%, respectively). The electron-transfer rates obtained for the systems $[Co\ dipy_3]^{3+}$–$[Co\ dipy_3]^{2+}$ at 45° and $[Co\ phen]^{3+}$–$[Co\ phen_3]^{2+}$ at 20° were 1120 and 268 mole^{-1} l. min.$^{-1}$, respectively.* No absolute quantitative reliance can be placed on these results in view of the assumed order-dependence for the electron-transfer process and because of the difficulty of reproducing similar amounts of impurity in all the runs. It did not seem worth while to extend these experiments in view of these difficulties and since direct exchange studies were in progress.[15] The observed catalysis by cobalt(II) also requires that both cobalt(II) complexes are labile, a result which has been observed in separate studies.[16]

Electron transfers between cobalt-(II) and -(III) complexes are almost invariably slow.[14,17] This has been explained by supposing that after the rapid electron transfer cobalt(III) is in a markedly different cobalt(II) environment and further readjustment is improbable. With complexes of such ligands as phenanthroline or dipyridyl however [which "produce" or "almost produce" a spin-paired cobalt(II) complex] this readjustment of environment may be eased, leading to rapid electron transfer, as observed.[18] It appears that most single-electron transfers involving phenanthroline and dipyridyl complexes are fast; [14,19] in some fashion the process is made easier by the presence of the π-electron cloud of the aromatic ligands.

These results emphasise the possible importance of traces of impurities in exchange reactions. In other investigations, enhancement of exchange rates has been ascribed to the presence of small amounts of chemical species.[4] In the present work the addition of a small amount of cerium(IV) [but not persulphate which decomposed the cobalt(II) complex] completely inhibited the neutral exchange (run 9). However, a product obtained by recrystallisation from a solution containing cerium(IV) (D5, run 10) still underwent exchange but the exchange was inhibited by the addition of cerium(IV). There is no question of the cerium's oxidising dipyridyl or forming a complex with it and thus removing it from the exchange mixture since dipyridyl can be extracted from the solution at the end of the experiment. The attempt similarly to quench the exchange with the phenanthroline complexes was vitiated by extensive oxidation of the phenanthroline by cerium(IV). It appears that it is easier to prepare the dipyridyl complex purer than the phenanthroline complex and as might have been expected the product from cobalt(III) reactants is purer than that involving oxidation of cobalt(II) complexes.

No exchange of $[Co\ en_3]^{3+}$ with [^{14}C]ethylenediamine is observed in 55 hours' refluxing in neutral aqueous solution.[20] Obviously cobalt(II) impurities are absent from these

* *Note Added, September 23rd*, 1957.—The rate of electron transfer between $[Co\ phen_3]^{3+}$ and $[Co\ phen_3]^{2+}$ is of first order in each reactant in nitrate media, and from measurements at 0° and 4·2° a rate constant of 215 mole^{-1} l. min.$^{-1}$ is estimated.[15] The agreement with our value is good, the difference in ionic strength being considered.

[15] Neumann and Baker, personal communication.
[16] Ellis and Wilkins, unpublished work.
[17] Adamson, *Rec. Trav. Chim.*, 1956, **75**, 291.
[18] Orgel, 10th Solvay Conference, Brussels, May, 1956.
[19] George and Irvine, *J.*, 1954, 587.
[20] Popplewell and Wilkins, unpublished work.

experiments since otherwise the slow (but measurable) $[Co\ en_3]^{2+}$–$[Co\ en_3]^{3+}$ electron-transfer process [21] combined with the known lability of $[Co\ en_3]^{2+}$ would have led to very slow exchange with this system in a similar way to that described above. Finally, the observed inertness of $[Co\ phen_3]^{3+}$ and $[Co\ dipy]^{3+}$ is easily understood on the basis that it is a diamagnetic " inner-orbital " complex.[3]

We are grateful to the Department of Scientific and Industrial Research for a maintenance allowance (to M. J. G. W.) and to the University of Sheffield for an Alfred Tongue Scholarship (to P. E.). We also thank Professor H. Neumann and Mr. B. Baker for preliminary information regarding the electron-transfer reaction.

THE UNIVERSITY, SHEFFIELD. [*Received, April 16th*, 1957.]

[21] Lewis, Coryell, and Irvine, *J.*, 1949, S386.

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899. *Urea and Related Compounds. Part IV.* Some Aromatic and Aliphatic Dithioformamidines.*

By FREDERICK KURZER and PHYLLIS M. SANDERSON.

Di-*ortho*-substituted arylthioureas are readily oxidised by bromine or hydrogen peroxide to diaryldithioformamidines, which are isolated in the form of their salts.

The preparation of dialkyl- and tetra-alkyl-dithioformamidine salts by this general reaction is also described.

IT is well known that thiourea is easily converted into dithioformamidine (I; R = H) by a variety of oxidising agents. This general reaction is applicable to *N*-alkylthioureas, several of which have been successfully oxidised to *N*-alkylated dithioformamides.[1–5] Aromatic thioureas, on the other hand, display a markedly different behaviour, yielding heterocylic products on treatment with the same oxidising agents. In general, benzothiazoles (II) are produced in non-polar media,[6–9] but " Hector's bases " † (III) result in ionising solvents, particularly in the presence of mineral acids.[10]

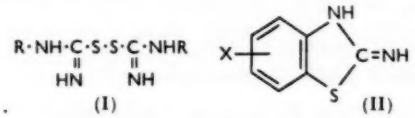
All previous efforts to obtain aromatic dithioformamidines appear to have been unsuccessful or inconclusive. The closest approach is Fichter and Braun's [2] general electrolytic method of oxidising thioureas to dithioformamidines. Their product from phenylthiourea, formulated as *s*-diphenyldithioformamidine hydrochloride, was however instantly decomposed in contact with water and could not be isolated in the pure state. Claims for the production of aromatic dithioformamidines by purely chemical methods have invariably proved erroneous. 2-Iminobenzothiazoline was first [11] formulated as the disulphide (I; R = Ph) and only later [7] correctly identified (as II; X = H). Fromm and Heyder's [12] efforts to synthesise *s*-diphenyldithioformamidine by using toluene-*p*-sulphonyl

* Part III, *J.*, 1953, 3360.

† In common with accepted practice, Hector's bases are represented, in the present paper, as 2 : 4-diaryl-3 : 5-di-imino-1 : 2 : 4-thiadiazolidines (III), although conclusive proof of this formulation has yet to be provided.

[1] Hector, *J. prakt. Chem.*, 1891, **44**, 492.
[2] Fichter and Braun, *Ber.*, 1914, **47**, 1529.
[3] (*a*) Lecher, Graf, Heuck, Köberle, Gnädiger, and Heydweiller, *Annalen*, 1925, **445**, 35; (*b*) Sahasrabudhey, *J. Indian Chem. Soc.*, 1951, **28**, 341.
[4] Klöping and van der Kerk, *Rec. Trav. chim.*, 1951, **70**, 917.
[5] Sahasrabudhey and Singh, *J. Indian Chem. Soc.*, 1952, **29**, 636.
[6] Fischer and Besthorn, *Annalen*, 1882, **212**, 326; Besthorn, *Ber.*, 1910, **43**, 1519; Hunter, *J.*, 1926, 1386.
[7] Hugershoff, *Ber.*, 1903, **36**, 3121, 3134; 1906, **39**, 1014.
[8] Sahasrabudhey and Krall, *J. Indian Chem. Soc.*, 1944, **21**, 17.
[9] Passing, *J. prakt. Chem.*, 1939, **153**, 10.
[10] For references see Kurzer, *J.*, 1955, 1.
[11] Hugershoff, *Ber.*, 1901, **34**, 3130.
[12] Fromm and Heyder, *Ber.*, 1909, **42**, 3804.

chloride as oxidising agent gave 3 : 5-di-imino-2 : 4-diphenyl-1 : 2 : 4-thiadiazolidine. Similarly, the alleged " disulphides " resulting in the sulphur monochloride-[13] or nitrous acid-oxidation[14] of *N*-methyl-*N*-phenylthiourea were recognised, in due course, as 2-imino-2-methylbenzothiazoline,[8] and the appropriate thiadiazolidine,[15] respectively. *N*-Methyl-*N'*-phenylthiourea, on treatment with nitrous acid, failed to yield a dithioformamidine,[16] as did *NN'*-diphenylthiourea which was studied in detail by Fromm.[17] Sahasrabudhey and Krall[15] were in fact thus led to the conclusion " that arylthiocarbamides do not yield disulphides on oxidation." On the other hand, aromatic dithioformamidines have frequently been assumed[1,2,12,18] to be involved as primary intermediates in the oxidation of arylthioureas to Hector's bases; indirect experiments have failed, however, to confirm or definitely refute this hypothesis.[15,17,19] Our first aim, therefore, in the present work was to isolate aromatic dithioformamidines (I; R = Ar) in some suitable form.



(I) (II) (III)

The oxidation of aromatic thioureas to 2-iminobenzothiazolines necessitates the elimination of the *o*-hydrogen atom. It seemed probable, therefore, that blocking of both *ortho*-positions with substituents would make the synthesis of the desired disulphides (I) feasible: our experiments confirmed this. 2 : 6-Dimethylphenylthiourea, on treatment with the theoretical quantity of bromine in a neutral solvent, afforded excellent yields of the corresponding dithioformamidine hydrobromide. With proper care, this could be isolated as such, or converted into other salts (including the toluene-*p*-sulphonate and picrate). 2 : 4 : 6-Tribromophenylthiourea gave comparable results.

Under the influence of hydrogen peroxide, the oxidation took one of several paths, which could be selected by a choice of the appropriate conditions. *s*-Di-(2 : 6-dimethylphenyl)dithioformamidine (I; R = 2 : 6-$C_6H_3Me_2$) hydrobromide was readily obtained in 75% yield when the thiourea was treated with the calculated quantity of the reagent at 0°, in the presence of a large excess of hydrobromic acid. In hot alcoholic media containing mineral acid [*i.e.*, under conditions that normally promote the formation of thiadiazolidines (III) in the aromatic series[10]], the peroxide merely desulphurised the starting material to 2 : 6-dimethylphenylurea (60%), while the expected thiadiazolidine (III; R = 2 : 6-$C_6H_3Me_2$) arose in only minute yields (4%). Meanwhile, in another connexion, an improved procedure for oxidising phenylthiourea had been evolved (use of perhydrol in absolute ethanol[20]) which raised the yield of Hector's base (III; R = Ph) from the usual 40—50% to 80—90%. Application of this modified procedure to the present case, though increasing the yields of 3 : 5-di-(2 : 6-dimethylphenyl)-2 : 4-di-imino-1 : 2 : 4-thiadiazolidine (III; R = 2 : 6-$C_6H_3Me_2$) (to 8—15%), resulted also in larger quantities (25—35%) of the by-product *NN'*-di-(2 : 6-dimethylphenyl)guanidine. *NN'*-Diarylguanidines are the chief products of the hydrolytic and reductive degradation[21] of Hector's bases; further, *s*-triphenylguanidine, instead of the expected thiadiazolidine, becomes the main product when *NN'*-diphenylthiourea is more vigorously oxidised.[17] The present observations fall in line with this general experience, although the exceptionally low yields of the thiadiazolidine may partly be due to steric effects.

[13] Dost, *Ber.*, 1906, **39**, 1014.
[14] Lal and Krall, *J. Indian Chem. Soc.*, 1937, **14**, 478.
[15] Sahasrabudhey and Krall, *ibid.*, 1945, **22**, 37.
[16] Lal and Krall, *ibid.*, 1938, **15**, 217.
[17] Fromm, *Annalen*, 1913, **394**, 284.
[18] De and Chakravarty, *J. Indian Chem. Soc.*, 1928, **5**, 661.
[19] Lal and Krall, *ibid.*, 1939, **16**, 31.
[20] Kurzer and Sanderson, unpublished work.
[21] Hector, *Oefvers. Kongl. Vet. Akad.*, 1892, 83 (cf. *Ber.*, 1892, **25**, ref. 799).

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Like all other dithioformamidines, the *s*-diaryl-homologues were incapable of existing as the free bases; they decomposed instantly with elimination of sulphur when attempts were made to liberate them from their salts by alkalis or alkali carbonates. The salts themselves, being sensitive to hydrolysis, were also labile: aqueous or ethanolic solutions of the hydrobromide or toluene-*p*-sulphonate of (I; R = 2 : 6-$C_6H_3Me_2$), for example, slowly deposited colloidal sulphur on storage when cold, and more rapidly when heated. The presence of a small excess of mineral acid stabilised such aqueous solutions, which then remained clear even at higher temperatures. Aryldithioformamidine salts were successfully crystallised, though not without difficulty, from suitable mixtures of solvents in the cold; unlike their aliphatic analogues (see below), they invariably formed dihydrates. The correctness of their structure (I), supported by their composition and the bromine uptake during their formation, was also confirmed by reductive hydrolysis; zinc and hydrochloric acid reconverted *s*-di-(2 : 6-dimethylphenyl)dithioformamidine almost quantitatively into the original thiourea.

Both methods of oxidising thioureas were finally extended to the synthesis of a series of new *s*-di- and tetra-alkyldithioformamidines (Alk = Me or Et) hydrobromides and picrates. The use of hydrogen peroxide at low temperatures, in conjunction with an excess of hydrobromic acid, added to suppress hydrolysis of the products, is a convenient general procedure for preparing alkyl homologues in this series. Hector [1] has reported the formation of diallyldithioformamidine by oxidation of the thiourea with acidified hydrogen peroxide at its boiling point. Since sulphur was deposited during the oxidation, and the alleged " free base " was isolated after treatment that is now known to decompose dithioformamidines (see ref. 2), this claim must be set aside. Bromine in chloroform has recently been used in oxidising *NN*-dimethylthiourea, but the product was incorrectly formulated.[5] The present experiments have shown that the halogen uptake is accelerated remarkably in the presence of water, which was therefore preferred as solvent for the thioureas. In their properties, the alkyldithioformamidines resembled the aromatic analogues; their salts were equally or even more labile.

A number of new substituted ureas and thioureas required in this work were prepared by suitable modifications of standard methods. *NN*-Dimethyl- and -diethyl-thiourea, previously synthesised by Wallach [22,23] from the dialkylcyanamide and ammoniacal ethanolic hydrogen sulphide, have now been obtained more conveniently by the use of Fairfull, Lowe, and Peak's excellent general procedure [24] of adding the elements of hydrogen sulphide to the cyano-group. 2 : 6-Dimethylphenyl-urea and -thiourea were produced without difficulty from 2 : 6-dimethylaniline by the action of cyanic and thiocyanic acid, respectively.[25] This urea displayed to a large degree, even below its melting point, the general tendency of arylureas to disproportionate into *s*-diarylureas.[26] Since its physical properties were therefore difficult to determine, it was converted, for identification, into sulphonylcyanamides almost quantitatively by the usual method.[27] 2 : 6-Dimethylphenylthiourea gave an addition compound with zinc chloride which proved useful in the isolation of the thiourea obtained in zinc-reduction experiments. The general method of preparing and isomerising the amine thiocyanate proved inapplicable to the synthesis of 2 : 4 : 6-tribromophenylthiourea, presumably because of the low basicity * of the tribromoaniline. Although the thiourea was obtainable by this reaction by employing Passing's

* Although figures for a direct comparison of the basicity of 2 : 6-dimethyl- and 2 : 4 : 6-tribromoaniline are not available, the lower basic strengths of bromine derivatives are clearly shown by the dissociation constants of the following anilines: *p*-methyl, 20×10^{-10}; *p*-bromo, $0{\cdot}2 \times 10^{-10}$; *o*-methyl, 3×10^{-10}; *o*-bromo, $0{\cdot}01 \times 10^{-10}$.

[22] Wallach, *Ber.*, 1899, **32**, 1874.
[23] Preisler, *J. Amer. Chem. Soc.*, 1949, **71**, 2849.
[24] Fairfull, Low, and Peak, *J.*, 1952, 742.
[25] Kurzer, *Org. Synth.*, 1951, **31**, 8, 21.
[26] Kurzer, *J.*, 1949, 2292.
[27] Kurzer, *J.*, 1949, 1034, 3029.

experimental modification [9] (interaction of suspended amine hydrochloride and ammonium thiocyanate in boiling chlorobenzene) yields were erratic and low. The thiourea was finally synthesised in consistently excellent yield by Frank and Smith's method,[28] involving condensation of 2 : 4 : 6-tribromoaniline with benzoyl *iso*thiocyanate prepared *in situ*, followed by the hydrolytic removal of the benzoyl group from the intermediate *N*-acyl-*N'*-arylthiourea.

Experimental

Bromide in dithioformamidine hydrobromides was estimated volumetrically by Volhard's method on specimens (approx. 0·2 g.) dissolved in cold water, with addition of a few drops of 3N-nitric acid. Since warming such solutions was inadmissible (separation of silver sulphide), the need for coagulating and removing the precipitated silver bromide was avoided by the use of nitrobenzene.

Contact of wet dithioformamidine salts with metal spatulas is to be avoided to prevent local decomposition.

In the preparation of dithioformamidine picrates, aqueous picric acid, saturated at 30° (containing 0·06 mole of the reactant per l.[29]), was employed.

Aromatic Dithioformamidines

2 : 6-*Dimethylphenylurea*.—A solution of 2 : 6-dimethylaniline (36 g., 0·3 mole) in acetic acid (150 ml.), diluted with water (100 ml.), was treated with an aqueous suspension of sodium cyanate (39 g., 0·6 mole, in 100 ml.) with very vigorous stirring at room temperature. The crude urea separated immediately with slight warming and frothing and formed a paste-like suspension, which was set aside for several hours. The product was collected, washed with water, and consisted of white crystalline 2 : 6-*dimethylphenylurea* (42 g., 85%). Recrystallisation from aqueous ethanol (ethanol, 25 ml., and water, 5 ml., per g.) gave felted needles (Found: C, 65·8; H, 7·4. $C_9H_{12}ON_2$ requires C, 65·85; H, 7·3%). The urea changes to the *NN'*-diarylurea below its m. p. and hence does not melt when slowly heated. When determined by the " inverted " procedure,[26] the m. p. was found to be between 242° and 236°.

N-*Benzenesulphonyl*-N-(2 : 6-*dimethylphenyl*)*cyanamide*.—2 : 6-Dimethylphenylurea (8·2 g., 0·05 mole) in pyridine (45 ml.) was treated with benzenesulphonyl chloride (26·4 g., 0·15 mole), and the resulting hot liquid set aside during 15 min. and poured into acidified ice-water (300 ml.). The resulting solidified oil gave, after three crystallisations from acetone–ethanol–water (1, 2, and 0·5 ml. respectively, per g.), prisms of the *cyanamide*, m. p. 106—108° (85%) (Found: C, 62·3; H, 4·6; N, 9·9. $C_{15}H_{14}O_2N_2S$ requires C, 62·9; H, 4·9; N, 9·8%). N-(2 : 6-*Dimethylphenyl*)-N-*toluene*-p-*sulphonylcyanamide*, similarly prepared [27] in 90% yield, consisted of glass-like prisms, m. p. 131—132° (from aqueous ethanol–acetone) (Found: C, 63·7; H, 5·3. $C_{16}H_{16}O_2N_2S$ requires C, 64·0; H, 5·3%). Small quantities of unchanged 2 : 6-dimethylphenylurea were recovered as fractions sparingly soluble in acetone, in both experiments.

2 : 6-*Dimethylphenylthiourea*.—A solution of 2 : 6-dimethylaniline (60·5 g., 0·5 mole) in 1·5N-hydrochloric acid (500 ml., 0·75 mole) was treated with ammonium thiocyanate (76 g., 1 mole), and the liquid was kept at 100° during 1 hr. and then allowed to cool to room temperature. Evaporation on the steam-bath (4 hr.) gave a yellow residue which was kept at 100° for a further 8 hr. The powdered solid was extracted with warm water, and the residual white powder (80 g., 89%) twice crystallised from boiling ethanol (400 ml.), needles of 2 : 6-dimethylphenylthiourea, m. p. 202—204°, being obtained (Found: C, 59·9; H, 6·6. Calc. for $C_9H_{12}N_2S$: C, 60·0; H, 6·7%). The compound has previously been prepared from the *iso*thiocyanate and ammonia, but the m. p. given was 190°.[30]

2 : 4 : 6-*Tribromophenylthiourea*.—(*a*) A solution of 2 : 4 : 6-tribromoaniline (49·5 g., 0·15 mole) in warm anhydrous chlorobenzene (150 ml.) was rapidly treated with hydrogen chloride (approx. 6·5 l., 0·3 mole) until separation of the hydrochloride was complete. To the white paste, finely powdered ammonium thiocyanate (58 g., 0·75 mole, previously dried at 80° during 2 hr.) was added. The stirred mixture was heated to 100° during the first hour, then gently boiled under reflux. Small quantities of a dark orange oil that had first separated redissolved, and the suspended material changed gradually to a pale yellow powder, while some hydrogen

[28] Frank and Smith, *Org. Synth.*, Coll. Vol. III, p. 735 (1955).
[29] Dolinski, *Ber.*, 1905, **38**, 1836.
[30] Dyson, George, and Hunter, *J.*, 1927, 436.

sulphide was evolved. After 4 hours' refluxing, the solid was quickly filtered off with suction (filtrate A) and rinsed with a little chlorobenzene. After being suspended in water to remove ammonium salts, the crude product (dry weight 20—24 g., 34—41%) was crystallised by dissolution in boiling acetone (25—30 ml. per g.), distillation of the filtered liquid to about half-bulk, and dilution with ethanol (10 ml. per g.). Two crystallisations gave prisms of 2 : 4 : 6-*tribromophenylthiourea*, m. p. 240—242° (decomp.) (Found: C, 22·2; H, 1·6; N, 7·05; S, 8·2; Br, 62·0. $C_7H_5N_2Br_3S$ requires C, 21·6; H, 1·3; N, 7·2; S, 8·2; Br, 61·7%).

Most of the unconverted starting material contained in filtrate (A) separated when the liquid was distilled to small bulk. The use of a smaller excess of ammonium thiocyanate (2 mols.) reduced the yield to 7—10%.

(*b*) Benzoyl chloride (14·1 g., 0·1 mole) was run into a stirred solution of ammonium thiocyanate (8·5 g., 0·11 mole) in anhydrous acetone (50 ml.) during 5 min., and the resulting suspension refluxed during a further 5 min. A solution of 2 : 4 : 6-tribromoaniline (33·0 g., 0·1 mole) in nearly boiling acetone (150 ml.) was next added during 10 min., and the stirred yellow suspension refluxed during another 45 min. Its addition to ice-water (750 ml.) produced a yellow precipitate of crude *N*-benzoyl-*N'*-2 : 4 : 6-tribromophenylthiourea, which was collected and immediately boiled with 3N-sodium hydroxide (180 ml.) during 6 min. The resulting liquid was decanted from a small quantity of undissolved residue (3—6 g., consisting of crude 2 : 4 : 6-tribromoaniline, m. p. and mixed m. p. 118—119°, after crystallisation from ethanol), diluted with ice (to a total volume of 300 ml.), stirred with carbon (3 g.), and filtered at the pump. The clear filtrate gave, on acidification with concentrated hydrochloric acid (to Congo-red), a white crystalline precipitate, which was collected at 0°, washed with water (dry wt., 40—45 g.), and crystallised as above, affording colourless prisms of 2 : 4 : 6-tribromophenylthiourea, m. p. 240—242° (decomp.) (yield, including good material from the mother-liquors, 25·3—29·2 g., 65—75%) (Found: C, 22·0; H, 1·4; Br, 61·3%).

s-*Bis*-(2 : 6-*dimethylphenyl*)*dithioformamidine*.—(a) *Bromine oxidation*. Finely divided 2 : 6-dimethylphenylthiourea (3·60 g., 0·02-mole), suspended in chloroform (35 ml.), was treated dropwise, with external ice-cooling, with M-bromine in chloroform (10 ml., 0·01 mole). The resulting clear colourless liquid was rapidly evaporated in a vacuum at room temperature, the residual solid dissolved in water (10, 5, and 5 ml.), and the solution separated from a drop of chloroform (liquid A) if necessary, and filtered (Filtrate F).

Hydrobromide. To the clear filtrate (F), cold saturated, aqueous sodium bromide (0·02 mole) was slowly added with external cooling, until a faint turbidity appeared; the crystalline material which separated on storage at room temperature was collected, quickly washed with the minimum of ice-water, then with ether, and dried in a vacuum. It consisted of white prisms (4·45 g., 80%) of s-*bis*-(2 : 6-*dimethylphenyl*)*dithioformamidine dihydrobromide dihydrate*, m. p.* 127—128° (decomp., after sintering at 125°) (Found: C, 38·2; H, 4·8; N, 10·3; S, 11·8; Br, 29·5, 29·8. $C_{18}H_{22}N_4S_2,2HBr,2H_2O$ requires C, 38·9; H, 5·0; N, 10·1; S, 11·5; Br, 28·75%). The dihydrobromide was crystallised by being dissolved in *cold* ethanol (15 ml.); the solution, acidified with 60% hydrobromic acid (2 drops) and filtered if necessary, was slowly diluted with ether (12 ml.); the crystalline product, m. p. 129—130° (after sintering at 125°), was collected at 0° and rinsed with 1 : 2 ethanol–ether (recovery, approx. 75%). The salt was stable in aqueous solution, even on warming, if acidified with little mineral acid. Its aqueous solution deposited colloidal sulphur instantly on being made alkaline, and more slowly on being heated.

Liquid A consisted of a solution of traces of starting material in chloroform.

Alternatively, filtrate F was slowly treated, with external cooling, with 60% hydrobromic acid (5 ml.), and the separated dihydrobromide (m. p.* 130—132°, after sintering at 128°; 4·15 g., 75%) collected after storage at 0° (Found: C, 38·5; H, 5·0; Br, 29·5%).

Toluene-p-*sulphonate*. Filtrate F was treated with toluene-*p*-sulphonic acid monohydrate (3·80 g., 0·02 mole) dissolved in water (5 ml.). The resulting white precipitate was collected after storage at 0°, washed with little ether, and air-dried at room-temperature [m. p. 112—114° (decomp.); 6·20 g., 84%]. If crystallisation was desired, the *freshly* collected filter-cake was suspended in cold ethanol (25 ml.) and dissolved by prolonged stirring, and the filtered solution (vacuum) slowly diluted with ether (150—180 ml.) and stored at −8°. The collected

* The m. p. of the hydrobromide obtained by the addition of sodium bromide was slightly lower than that of specimens separated by the use of hydrobromic acid, probably because of the difficulty of completely removing the sodium bromide without redissolving the desired product.

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prisms (2·65 g., 36%) were s-*bis*-(2 : 6-*dimethylphenyl*)*dithioformamidine ditoluene*-p-*sulphonate dihydrate*, m. p. 116—117° (decomp.) (Found: C, 52·1, 51·8; H, 5·9, 5·5; S, 17·7. $C_{18}H_{22}N_4S_2,2C_7H_8O_3S,2H_2O$ requires C, 52·0; H, 5·7; S, 17·3%). The salt decomposed with deposition of sulphur when its ethanolic solution was boiled, or its aqueous solution was basified or heated (except in the presence of mineral acid).

Addition of *m*-nitrobenzenesulphonic acid (0·02 mole) in water (15 ml.) to filtrate (F) gave an almost colourless oil (4—5 ml.) which was highly soluble in the usual organic solvents and did not crystallise therefrom. Benzenesulphonic acid, analogously, gave a minute quantity of oil. The filtrate F did not deposit salts on being treated with salicylsulphonic, oxalic or succinic acid.

Picrate. Filtrate F was slowly stirred into aqueous picric acid (0·018 mole). The yellow crystalline precipitate, collected at 0° and dried at room temperature in a vacuum over phosphoric oxide (yield, 5·80 g., 68%), was the *dipicrate dihydrate*, m. p. 92—94° (decomp.) (Found: C, 42·6; H, 3·8. $C_{18}H_{22}N_4S_2,2C_6H_3O_7N_3,2H_2O$ requires C, 42·25; H, 3·8%). Dissolution of this product in cold methanol–acetone (1 : 2; 3 ml. per g.), followed by dropwise dilution of the filtered liquid with water (6—8 drops per g.), gave lemon-yellow prisms (recovery, 50%) of the anhydrous *dipicrate*, m. p. 105—107° (decomp., after sintering at 101—103°) (Found: C, 44·6; H, 3·4; N, 16·8. $C_{18}H_{22}N_4S_2,2C_6H_3O_7N_3$ requires C, 44·1; H, 3·4; N, 17·2%).

(b) *Hydrogen peroxide oxidation.* A suspension of 2 : 6-dimethylphenylthiourea (3·6 g.; 0·02 mole) in water (10 ml.) and 60% hydrobromic acid (5 ml.) was shaken, at 0°, with 6% hydrogen peroxide (6·2 ml., 0·011 mole) during 10—15 min. Almost complete dissolution occurred at one stage, and separation of the salt was completed, as far as possible, by addition of ethanol (5 ml.) and storage at 0°. The collected product (4·2 g., 75%) was *s*-bis-(2 : 6-dimethylphenyl)dithioformamidine dihydrobromide dihydrate, m. p. and mixed m. p. 130—132° after sintering at 127°).

(c) *Reductive hydrolysis.* A boiling solution of *s*-bis-(2 : 6-dimethylphenyl)dithioformamidine dihydrobromide dihydrate (2·78 g., 0·005 mole) in ethanol (25 ml.) containing concentrated hydrochloric acid (1 drop) was treated with zinc foil (4 g.), followed by concentrated hydrochloric acid (4 ml., added during 10 min.), and the effervescing suspension refluxed during 0·5 hr. The liquid was decanted, the residual zinc re-extracted with 85% ethanol (2 × 5 ml.), and the combined extracts were filtered hot. They deposited crystals (m. p. 235—236°, 1·9 g.) on cooling, and more of the same product (0·5 g., *i.e.*, total 93%) on partial evaporation. Crystallisation from 85% ethanol gave white prisms of 2 : 6-*dimethylphenylthiourea–zinc chloride hydrate*, m. p. 238—240° (decomp.) (Found: C, 41·6; H, 4·9; S, 12·8; Cl, 14·1. $2C_9H_{12}N_2S,ZnCl_2,H_2O$ requires C, 42·0; N, 5·05; S, 12·4; Cl, 13·8%).

The same product was obtained (92%) when equimolar quantities of 2 : 6-dimethylphenylthiourea (in hot ethanol) and zinc chloride (in water) were mixed.

s-*Bis*-(2 : 4 : 6-*tribromophenyl*)*dithioformamidine*.—A suspension of finely divided 2 : 4 : 6-tribromophenylthiourea (1·95 g., 0·005 mole) in chloroform (50 ml.) containing water (2 ml.) was continuously ground in a mortar, while 0·1M-bromine in chloroform (25 ml., 0·0025 mole) was added dropwise during 10—15 min. The crystalline starting material was thereby converted into a suspended white microgranular solid which was collected at the pump, washed with chloroform, and dried in a vacuum (2·13 g., 88%). It consisted of s-*bis*-(2 : 4 : 6-*tribromophenyl*)*dithioformamidine dihydrobromide dihydrate*, m. p. 160—162° (decomp., after sintering at 156°) (Found: C, 17·5; H, 1·5; N, 5·8; Br, 65·2. $C_{14}H_8N_4S_2Br_6,2HBr,2H_2O$ requires C, 17·3; H, 1·4; N, 5·75; Br, 65·7%). Addition of water appears to prevent the formation of local orange agglomerates of brominated material.

Oxidation of 2 : 6-*Dimethylphenylthiourea by Hydrogen Peroxide.*—(a) *Desulphurisation.* A boiling solution of 2 : 6-dimethylphenylthiourea (1·80 g., 0·01 mole) in ethanol (12 ml.) and water (4 ml.), containing concentrated hydrochloric acid (0·5 ml., 0·005 mole) was treated with 6% hydrogen peroxide (8·5 ml., 0·015 mole) during 2—3 min. The resulting turbid liquid, containing precipitated sulphur, was boiled for a further 6 min., and the nearly clarified solution decanted from the sulphur, stirred into water (50 m.), and made just alkaline with 3N-aqueous ammonia. The crystalline precipitate, collected at 0° (1·37 g.) (filtrate A), gave, after crystallisation from ethanol–water (5 : 1), needles of 2 : 6-dimethylphenylurea [the identity of which was established by its almost quantitative conversion into *N*-(2 : 6-dimethylphenyl)-*N*-toluene-*p*-sulphonylcyanamide, m. p. and mixed m. p. 131—132°]. The alcoholic mother-liquors therefrom were allowed to evaporate to dryness and the residue extracted with cold 3N-hydrochloric

acid (3 × 5 ml.). The small insoluble residue consisted of more 2 : 6-dimethylphenylurea; basification of the acid extracts precipitated a mixture of 3 : 5-di-(2 : 6-dimethylphenyl)-2 : 4-di-imino-1 : 2 : 4-thiadiazolidine (0·06 g., 4%) and *NN'*-di-(2 : 6-dimethylphenyl)guanidine (0·2 g., 12%) which were separated and identified as described in section (b). Evaporation of the aqueous filtrate A gave a further small fraction of 2 : 6-dimethylphenylurea (total, 0·98 g., 60%).

(b) 3 : 5-*Di*-(2 : 6-*dimethylphenyl*)-2 : 4-*di-imino*-1 : 2 : 4-*thiadiazolidine*. A boiling solution of the thiourea (0·02 mole) in ethanol (40 ml.) and concentrated hydrochloric acid (0·5 ml.) was treated with 30% hydrogen peroxide (2·5 ml., 0·022 mole) during 3—5 min. The liquid was boiled during another 5—8 min., decanted from the coagulated sulphur (0·3—0·45 g.), and stirred into water (250 ml.), and the precipitated solid collected at 0°. This was extracted with 3N-hydrochloric acid (3 × 5 ml.), and the undissolved 2 : 6-dimethylphenylurea (0·16—0·34 g., 5—10%) removed by filtration. Basification of the extracts gave a white solid (1·6—2·0 g.), which was dissolved in acetone–methanol (1 : 2). The separated product (filtrate F) [m. p. 229—230° (decomp.); 0·26—0·48 g., 8—15%] was recrystallised from the same solvents, and consisted of prisms of 3 : 5-*di*-(2 : 6-*dimethylphenyl*)-2 : 4-*di-imino*-1 : 2 : 4-*thiadiazolidine*, m. p. 226—228° (decomp.) (Found: C, 66·5; H, 5·8; N, 17·6; S, 10·1. $C_{18}H_{20}N_4S$ requires C, 66·7; H, 6·2; N, 17·3; S, 9·9%).

Gradual dilution of filtrates F with water precipitated a white solid (m. p. 95—98°; 0·83—1·16 g., 25—35%), which was crystallised by dissolution in ethanol and dilution with a little water, affording prisms of *NN'-di*-(2 : 6-*dimethylphenyl*)*guanidine*, m. p. 98—99° (Found: C, 68·6, 68·9; H, 8·2, 8·3; N, 13·2. $C_{17}H_{21}N_3,H_2O,C_2H_5OH$ requires C, 68·9; H, 8·8; N, 12·7%). Its *picrate*, prepared by the interaction of equimolar quantities of guanidine and picric acid in saturated ethanolic solution, and crystallised from ethanol, formed yellow platelets, m. p. 170—172° (Found: C, 47·8; H, 4·1; N, 17·0. $C_{17}H_{21}N_3,2C_6H_3N_3O_7$ requires C, 48·0; H, 3·7; N, 17·4%).

In marked contrast, phenylthiourea was converted, under the conditions of experiments (b), into 2 : 4-di-imino-3 : 5-diphenyl-1 : 2 : 4-thiadiazolidine consistently in 80—90% yield.

Interaction of the above thiadiazolidine (0·001 mole) with toluene-*p*-sulphonyl chloride (0·003 mole) in pyridine (5 ml.) at 100° during 0·5 hr. afforded nearly quantitatively its *mono-toluene*-p-*sulphonyl derivative*, m. p. 257—259° (from acetone) (Found: C, 62·4; H, 5·5. $C_{25}H_{26}O_5N_4S_2$ requires C, 62·8; H, 5·4%).

Aliphatic Dithioformamidines

NN-*Dimethylthiourea*.—Dry hydrogen sulphide was slowly passed through a solution of dimethylcyanamide (17·5 g., 0·25 mole) in anhydrous pyridine (35 ml.) and triethylamine (25·25 g., 0·25 mole), the temperature of which rose spontaneously and was kept at 60°. Much crystalline solid had separated after 0·5 hr., but passage of gas was continued during 2 hr. The mixture was diluted with light petroleum (50 ml.), and the prisms were collected at 0° (m. p. 158—160°; 18·7 g., 72%) and rinsed with light petroleum. Crystallisation from water gave prisms of *NN*-dimethylthiourea, m. p. 162—163°. (The m. p. is variously given between 155° and 164° in the literature.[5, 22, 23, 31])

NN-*Diethylthiourea*.—Treatment of diethylcyanamide (0·25 mole) as above during 5 hr. (an additional 0·125 mole of triethylamine being added after 2 hr.) gave a clear green liquid, which was stirred into concentrated hydrochloric acid (50 ml.) and ice (100 g.). The precipitated colourless prisms were collected at 0° (m. p. 100—101°; 18·5 g., 56%). Crystallisation from water gave prismatic *NN*-diethylthiourea, m. p. 101—102° (lit.,[22, 23] 101—102°).

s-*Diethyldithioformamidine*.—(a) *By bromine oxidation*. A suspension of ethylthiourea (2·08 g., 0·02 mole) in chloroform (20 ml.) at 0° slowly absorbed M-bromine (in chloroform) (10 ml., 0·01 mole), added to it in portions, with vigorous shaking, during 10—15 min. After the removal of the solvent at room temperature (vacuum), the white crystalline residue was dissolved in cold water (15 ml.), and the colourless liquid filtered (filtrate F).

Hydrobromide. Addition of 60% hydrobromic acid (5 ml.), followed by storage at 0°, gave a fine white precipitate, which was collected (4·25 cm. Buchner funnel) and washed successively with ethanol, ethanol–ether, and ether. The air-dried product [m. p. 184—187° (decomp.);

[31] Salkowski, *Ber.*, 1893, **26**, 2505; Schenk and von Graevenitz, *Z. physiol. Chem.*, 1924, **141**, 138; Birtwell, Curd, Hendry, and Rose, *J.*, 1948, 1645; Singh and Saikia, *J. Indian Chem. Soc.*, 1953, **30**, 695.

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2·75 g., 75%], purified by being redissolved in water (12—15 ml.), and separated by the addition of 60% hydrobromic acid, consisted of prisms (2 g.) of s-*diethyldithioformamidine dihydrobromide*, m. p. 185—187° (decomp., after sintering at 183°) (Found: C, 20·0; H, 4·2; N, 15·8; Br, 43·8. $C_6H_{14}N_4S_2,2HBr$ requires C, 19·6; H, 4·35; N, 15·2; Br, 43·45%). The salt was moderately soluble in hot ethanol (but slowly deposited sulphur on boiling), sparingly soluble in cold ethanol, and almost insoluble in ether.

Picrate. Treatment of filtrate F with aqueous picric acid (0·018 mole) gave a yellow crystalline precipitate, which, collected at 0°, consisted of the *dipicrate* (4·65 g.), m. p. 120—121° (decomp., after sintering at 116°) (Found: C, 32·8; H, 2·9; N, 20·7; S, 9·4. $C_6H_{14}N_4S_2,2C_6H_3O_7N_3$ requires C, 32·5; H, 3·0; N, 21·1; S, 9·6%). The material slowly deposited sulphur on being boiled in ethanol or methanol, but did not crystallise therefrom without partial decomposition.

Filtrate F remained clear after being treated with toluene-*p*-sulphonic acid (0·02 mole).

(b) *By hydrogen peroxide oxidation.* A suspension of ethylthiourea (2·08 g., 0·02 mole) in water (10 ml.) and 60% hydrobromic acid (1 ml.) was treated, during 10 min., with 6% hydrogen peroxide (6·2 ml., 0·011 mole), with shaking and external cooling to maintain the mixture below 30°. The resulting clear liquid, diluted with more 60% hydrobromic acid (5 ml.), deposited white crystalline *s*-diethyldithioformamidine dihydrobromide (1·8 g., 50%), m. p. and mixed m. p. 185—187°, which was collected after 24 hours' storage at 0°. Alternatively, the clear solution obtained by the above oxidation [but in the presence of concentrated hydrochloric acid (1 ml., 0·01 mole)], when treated with aqueous picric acid (0·018 mole), gave a precipitate (2·65 g., 40%) of *s*-diethyldithioformamidine dipicrate, m. p. and mixed m. p. 120—121° (decomp., after sintering at 116°).

s-*Dimethyldithioformamidine.—By bromine oxidation.* A solution of methylthiourea (1·80 g., 0·02 mole) in water (10 ml.) rapidly decolorised M-bromine in chloroform (10 ml., 0·01 mole). The resulting crystalline precipitate was redissolved by the addition of more water (10 ml.) and shaking, and the separated filtered aqueous layer (L) treated with 60% hydrobromic acid (5 ml.). The resulting crystals, collected at 0°, were successively washed with cold ethanol and ether, affording (1·50 g., 45%) felted needles of s-*dimethyldithioformamidine dihydrobromide*, m. p. 204—205° (Found: C, 14·3; H, 3·7; N, 16·0; Br, 47·15. $C_4H_{10}N_4S_2,2HBr$ requires C, 14·1; H, 3·5; N, 16·5; Br, 47·0%). Unlike the ethyl homologue, methylthiourea failed to decolorise bromine in chloroform, unless water was present.

Alternatively, solution L, treated with aqueous picric acid (0·018 mole), deposited yellow prisms (2·55 g., 40%) of the *dipicrate*, m. p. 119—120° (decomp.) (Found: C, 29·9; H, 2·3. $C_4H_{10}N_4S_2,2C_6H_3O_7N_3$ requires C, 30·2; H, 2·5%).

Oxidation of methylthiourea by hydrogen peroxide [as described for the ethyl homologue, except that the reactant was initially dissolved in 50% aqueous ethanol (10 ml.)] similarly afforded the above dihydrobromide, m. p. 204—206° (decomp.), and dipicrate, m. p. 119—120° (decomp.), in 60 and 45% yield, respectively.

Bis-(NN-*dimethyl*)*dithioformamidine.*—(i) *By bromine oxidation.* (*a*) A solution of *NN*-dimethylthiourea (2·08 g., 0·02 mole) in water (4 ml.) rapidly decolorised M-chloroformic bromine (0·01 mole), while a white solid appeared. After removal of the chloroform (at room temperature), the residual suspension was diluted with ethanol (5 ml.) and 60% hydrobromic acid (1 ml.), and the separated white crystalline tetramethyl derivative dihydrobromide (2·75 g.), m. p. 209—210° (decomp., after sintering at 205°), was collected at 0° and washed with ether (Found: C, 20·0; H, 4·3; N, 15·1; S, 16·9; Br, 43·9. Calc. for $C_6H_{14}N_4S_2,2HBr$: C, 19·6; H, 4·35; N, 15·2; S, 17·4; Br, 43·45%). The product was exceedingly water-soluble: purification by reprecipitation from saturated aqueous solution by 60% hydrobromic acid, ethanol, and ether was wasteful and did not raise the m. p.

(*b*) Oxidation as above, but followed by dissolution of the distilled residue in water (15 ml.) and treatment with picric acid (0·018 mole), gave the pale yellow *dipicrate*, m. p. 104—105° (decomp.) (4·67 g., 70%) (Found: C, 33·0; H, 3·0; N, 20·8. $C_6H_{14}N_4S_2,2C_6H_3O_7N_3$ requires C, 32·5; H, 3·0; N, 21·1%).

(ii) *By hydrogen peroxide oxidation.* A solution of the reactant (0·02 mole) in ethanol (10 ml.), diluted with 60% hydrobromic acid (1 ml.), was treated, with external cooling and shaking, with 30% hydrogen peroxide (1·25 ml., 0·011 mole), and the resulting dihydrobromide, m. p. and mixed m. p. 208—209°, collected at 0° (56%) (Found: C, 19·85; H, 4·5%). This variation of the usual conditions was necessitated by the high solubility of the salt in water.

Oxidation, by 6% hydrogen peroxide, as described for ethylthiourea, afforded the dipicrate (3·45 g., 52%), m. p. and mixed m. p. 104—105° (Found: C, 32·8; H, 2·95; N, 20·8%).

Bis-(NN-*diethyl*)*dithioformamidine*.—Oxidation of *NN*-diethylthiourea (2·64 g., 0·02 mole) by bromine or hydrogen peroxide (as described for the dimethyl homologue), and addition of picric acid (0·018 mole) gave pale yellow *bis*-(NN-*diethyl*)*dithioformamidine dipicrate*, m. p. 109—110° (decomp.) [Found: (*a*) C, 36·4; H, 3·6. (*b*) C, 36·7; H, 4·1; N, 19·4; S, 8·9. $C_{10}H_{22}N_4S_2,2C_6H_3O_7N_3$ requires C, 36·7; H, 3·9; N, 19·4; S, 8·9%] [yield, (*a*) 72%; (*b*) 56%]. Because of its high solubility, the dihydrobromide could not be isolated.

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[*Received, June 3rd*, 1957.]

900. *Cereal Gums. Part II.* The Constitution of an Araboxylan from Rye Flour.*

By G. O. ASPINALL and R. J. STURGEON.

A water-soluble polysaccharide isolated from rye flour gave on hydrolysis xylose (60%), arabinose (29%), and glucose (5%). From hydrolysis of the methylated polysaccharide, controlled acid hydrolysis of the polysaccharide, and quantitative estimation of xylose residues unattacked by periodate in the original and degraded polysaccharides it is concluded that this highly-branched araboxylan contains chains of 1 : 4-linked β-D-xylopyranose residues with approximately every second xylose residue carrying a terminal L-arabofuranose residue linked through position 3.

THE water-soluble gums isolated from cereal grains contain residues of D-glucose, D-xylose, and L-arabinose in varying proportions. Hexosan-rich and pentosan-rich fractions may be obtained either by graded precipitation from aqueous solution by ammonium sulphate [1,2] or by fractional precipitation of the derived acetylated polysaccharides.[3,4] The β-glucans from barley [5] and oats [6] are similar to lichenin [7] in structure in containing chains of 1 : 3- and 1 : 4-linked D-glucopyranose residues. The pentosan from wheat flour has been studied by Perlin [3] and by Montgomery and Smith.[4] The L-arabinose residues are present exclusively as non-reducing end-groups in the furanose form, and it is probable that these units are directly attached to a backbone of 1 : 4-linked β-D-xylopyranose residues. It has been shown by Preece and Hobkirk [2] that the main component of the water-soluble gum fraction from rye flour is an araboxylan of similar composition to the polysaccharide from wheat flour. We are very grateful to Professor I. A. Preece for kindly placing at our disposal a quantity of the rye araboxylan for structural investigation, the results of which are described in this paper.

The polysaccharide had a high negative rotation ($[\alpha]_D$ −107° in N-NaOH) and yielded on hydrolysis xylose (60%), arabinose (29%), and glucose (5·5%). Hydrolysis of the derived methylated polysaccharide afforded the following sugars, characterised by crystalline derivatives: 2 : 3 : 5-tri-*O*-methyl-L-arabinose (30%), 2 : 3-di-*O*-methyl-D-xylose (36%), 2-*O*-methyl-D-xylose (31%), and D-xylose (2·5%). In addition, chromatography showed traces of 2 : 3 : 4-tri-*O*-methylxylose, tri-*O*-methylglucose, and 3-*O*-methylxylose. These results indicate the presence in the polysaccharide of chains of 1 : 4-linked D-xylose residues with branching mainly through position 3. All the side-chains are terminated by L-arabofuranose residues, this being the sole mode of linkage of the arabinose residues. It is not certain whether the small amount of D-xylose isolated from the hydrolysis of the

* Part I, *J.*, 1954, 3519.

[1] Preece and Mackenzie, *J. Inst. Brewing*, 1952, **58**, 353, 457.
[2] Preece and Hobkirk, *ibid.*, 1953, **59**, 385.
[3] Perlin, *Cereal Chem.*, 1951, **28**, 370, 382.
[4] Montgomery and Smith, *J. Amer. Chem. Soc.*, 1955, **77**, 3325.
[5] Aspinall and Telfer, *J.*, 1954, 3519.
[6] Acker, Diemair, and Samhammer, *Z. Lebensm.-Untersuch.*, 1955, **100**, 180; **102**, 225.
[7] Chanda, Hirst, and Manners, *J.*, 1957, 1951.

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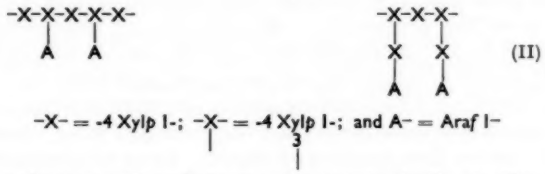
methylated polysaccharide represents some double branching points or whether the sugar arises from incomplete methylation of the polysaccharide or demethylation during hydrolysis. It is probable that the glucose residues present in the polysaccharide and the tri-*O*-methylglucose isolated on hydrolysis of the methylated polysaccharide arise from a contaminating glucan since no methyl ethers of glucose could be detected in the hydrolysate of another fraction of methylated polysaccharide.

On the basis of the methylation results two probable structures (I and II) may be put forward for the repeating unit of the polysaccharide. The following results provide evidence in favour of structure (I). Hydrolysis of the periodate-oxidised polysaccharide indicated the presence in the polysaccharide of xylose (24—25%) residues unattacked by periodate. This value is slightly lower than would be expected if all the arabinose residues were attached to singly branched xylose residues (*ca.* 29%). Controlled hydrolysis of the polysaccharide caused selective cleavage of some of the arabofuranosyl linkages with the formation of a degraded polysaccharide, giving on hydrolysis xylose (60%) and arabinose (10%) (these and subsequent values are expressed as percentages of the undegraded polysaccharide). Hydrolysis of the periodate-oxidised degraded polysaccharide indicated the presence therein of xylose (8%) residues unattacked by periodate. The reduction (*ca.* 16—17%) in xylose residues unattacked by periodate accompanying the controlled degradation of the polysaccharide corresponds approximately to the decrease (*ca.* 19%) in arabinose residues. This result would be expected on the basis of structure (I) only, and shows that the majority, at least, of the L-arabofuranosyl residues must be attached directly to position 3 of β-D-xylopyranose residues present in the essentially linear backbone of the molecule.



The araboxylan from rye flour is in many respects similar to the araboxylan from wheat flour,[3,4] notably in that the L-arabofuranose units, present only as end-groups, are attached directly to the backbone of 1 : 4-linked β-D-xylopyranose units. The main structural difference between the two polysaccharides lies in the mode of attachment of some of the arabofuranose residues. In the rye pentosan the majority at least of the arabinose residues are linked through $C_{(3)}$ of singly branched xylose residues, whereas in the wheat pentosan an appreciable proportion of arabinose residues are also linked through $C_{(2)}$ of doubly branched xylose residues. It is noteworthy that terminal L-arabofuranose units linked to $C_{(3)}$ of 1 : 4-linked β-D-xylopyranose units are commonly found in xylans from lignified tissues, especially of the *Gramineae*.[8]

Experimental

Paper partition chromatography was carried out on Whatman No. 1 filter paper with the following solvent systems (v/v): (A) butan-1-ol–benzene–pyridine–water (**5 : 1 : 3 : 3**, upper layer); (B) butan-1-ol–ethanol–water (**4 : 1 : 5**, upper layer); (C) benzene–ethanol–water (**169 : 47 : 15**, upper layer).

Rye araboxylan had $[\alpha]_D^{18}$ −107° (*c* 1·2 in N-NaOH); a sample was hydrolysed with N-sulphuric acid for 4 hr. at 100°, and chromatographic examination [9] of the hydrolysate in solvent A then showed the presence of xylose (60%), arabinose (29%), and glucose (5·5%).

Methylation of Rye Araboxylan.—The polysaccharide (2 g.) was methylated by successive additions of methyl sulphate and sodium hydroxide, and then with methyl iodide and silver oxide. The product (1·8 g.) was fractionated by dissolution in boiling chloroform–light petroleum (b. p. 60—80°), to give a main fraction (1·33 g.), soluble in chloroform–light petroleum

[8] Hirst, *J.*, 1955, 2974; Aspinall and Schwarz, *Ann. Reports*, 1955, **52**, 261.
[9] Flood, Hirst, and Jones, *J.*, 1948, 1679.

(3 : 7), which had $[\alpha]_D^{18}$ −113° (*c* 0·5 in $CHCl_3$) and was used in subsequent experiments (Found: OMe, 38·8%). Chromatography of the hydrolysate in solvent B showed tri-, di-, and mono-*O*-methylpentoses, together with smaller quantities of xylose and tri-*O*-methylglucose. A minor fraction (0·28 g.) of the methylated polysaccharide, soluble in chloroform–light petroleum (4 : 6), had $[\alpha]_D^{18}$ −121° (*c* 0·5 in $CHCl_3$), and chromatography of the hydrolysate showed the same pentose derivatives but no tri-*O*-methylglucose.

Hydrolysis of Methylated Araboxylan and Separation of Methylated Sugars.—The methylated polysaccharide (1·3 g.) was kept in N-hydrochloric acid (250 ml.) at 30° for 6 days, and the solution was then heated at 100° for 6 hr. After neutralisation with silver carbonate, concentration gave a syrupy mixture of sugars. The syrup (1·06 g.) was fractionated on cellulose (60 × 3 cm.) with light petroleum (b. p. 100—120°)–butan-1-ol (7 : 3) saturated with water as eluant to give five fractions.

Fraction 1. The syrup (273 mg.) had $[\alpha]_D^{18}$ −36·3° (*c* 0·45 in H_2O) (Found: OMe, 46·4. Calc. for $C_8H_{16}O_5$: OMe, 48·4%). Chromatography in solvent C showed 2 : 3 : 5-tri-*O*-methylarabinose and a trace of 2 : 3 : 4-tri-*O*-methylxylose, and demethylation gave arabinose and a trace of xylose. The major component was identified as 2 : 3 : 5-tri-*O*-methyl-L-arabinose by conversion into 2 : 3 : 5-tri-*O*-methyl-L-arabonamide, m. p. and mixed m. p. 130—132°.

Fraction 2. The syrup (105 mg.) had $[\alpha]_D^{18}$ +24·2° (*c* 0·44 in H_2O) (Found: OMe, 35·5. Calc. for $C_7H_{14}O_5$: OMe, 34·8%), and chromatography in solvent B showed 2 : 3-di-*O*-methylxylose and a small amount of tri-*O*-methylglucose. The syrup crystallised when seeded with 2 : 3-di-*O*-methyl-β-D-xylose and had m. p. and mixed m. p. 76—78°. The derived 2 : 3-di-*O*-methyl-*N*-phenyl-D-xylosylamine had m. p. and mixed m. p. 121—122°. Approximate calculation from optical rotation indicated the presence in the fraction of 102 mg. of di-*O*-methyl-D-xylose and 3 mg. of tri-*O*-methyl-D-glucose.

Fraction 3. The chromatographically pure sugar (199 mg.) crystallised when seeded with 2 : 3-di-*O*-methyl-β-D-xylose, and had m. p. and mixed m. p. 80—81° and $[\alpha]_D^{18}$ −20·1° ⟶ +22·6° (equil.) (*c* 0·35 in H_2O) (Found: OMe, 34·7. Calc. for $C_7H_{14}O_5$: OMe, 34·8%). The aniline derivative had m. p. and mixed m. p. 121—123°.

Fraction 4. The crystalline sugar (237 mg.), after recrystallisation from methanol–water, had m. p. and mixed m. p. (with 2-*O*-methyl-β-D-xylose) 130°, and $[\alpha]_D^{18}$ −9·5° ⟶ +35° (equil.) (*c* 0·75 in H_2O) (Found: OMe, 18·7. Calc. for $C_6H_{12}O_5$: OMe, 18·8%). Ionophoretic examination of the mother-liquors showed that a small amount of the 3-methyl ether was also present.

Fraction 5. The syrup (17 mg.) travelled on the chromatogram at the same rate as D-xylose, had $[\alpha]_D^{18}$ +18° (*c* 0·75 in H_2O), and was characterised by conversion into the di-*O*-benzylidene dimethyl acetal, m. p. and mixed m. p. 208—209°.

Estimation of Sugar Residues Unattacked by Periodate.—The polysaccharide (352 mg.) was dissolved in water (10 ml.), sodium metaperiodate (792 mg.) was added, and the solution set aside in the dark for 4 days. Excess of barium chloride solution was added, insoluble barium salts were filtered off, and the filtrate was dialysed for 3 days. Concentration of the solution to small volume and addition of acetone (10 vol.) precipitated the periodate-oxidised polysaccharide (190 mg.). Hydrolysis of this material with N-sulphuric acid for 4 hr. at 100° and chromatographic examination [9] of the hydrolysate, using galactose as reference sugar, showed the presence of xylose (24%).

The polysaccharide (502 mg.) was dissolved in 0·01N-oxalic acid (50 ml.) and heated on the boiling-water bath for 1·5 hr. Ethanol (5 vol.) was added to the cooled solution, and degraded polysaccharide (387 mg.) was precipitated. Chromatography of the supernatant liquor showed only arabinose. Hydrolysis of the degraded polysaccharide afforded xylose (60%) and arabinose (10%) (these and the subsequent value are expressed as percentages of the undegraded polysaccharide). The degraded polysaccharide was converted into the corresponding periodate-oxidised polysaccharide, hydrolysis of which with N-sulphuric acid for 4 hr. at 100°, followed by chromatography [9] of the hydrolysate, showed xylose (8%).

The authors thank Professor E. L. Hirst, F.R.S., for his interest and advice, Professor I. A. Preece for the supply of rye araboxylan, the Department of Scientific and Industrial Research for the award of a Maintenance Allowance (to R. J. S.), and the Rockefeller Foundation and Imperial Chemical Industries Limited for grants.

DEPARTMENT OF CHEMISTRY, UNIVERSITY OF EDINBURGH. [*Received, June 24th,* 1957.]

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901. *Polyfluoroalkyl Compounds of Silicon. Part IV.* Polyfluoroalkyl-silanes, -silicones, and -polysiloxanes derived from Perfluoroalkylethylenes or Vinylsilanes.†*

By A. M. Geyer, R. N. Haszeldine, (the late) K. Leedham, and R. J. Marklow.

Two methods of synthesis of polyfluoroalkylsilicon compounds are employed: (*a*) free-radical reaction of a compound containing an Si–H bond, *e.g.*, $SiHCl_3$, SiH_2Cl_2, $SiHMeCl_2$, $SiHMe(OEt)_2$, with a fluoro-olefin, *e.g.*, $CF_3{\cdot}CH{:}CH_2$; (*b*) free-radical addition of a polyfluoroalkyl iodide or bromide, *e.g.*, CF_3I, $CF_2Cl{\cdot}CFClI$, CF_2Br_2, to an alkenylsilicon compound, *e.g.*, $CH_2{:}CH{\cdot}SiCl_3$. Silicones and polysiloxanes such as $[CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}Si{\cdot}O_{1.5}]_n$, $[CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}SiMe{\cdot}O]_n$, $[(CF_3{\cdot}CH_2{\cdot}CH_2)_2Si{\cdot}O]_n$, $[C_3F_7{\cdot}CH_2{\cdot}CH_2{\cdot}SiMe{\cdot}O]_n$, $[CF_3{\cdot}CHMe{\cdot}CH_2{\cdot}SiMe{\cdot}O]_n$, $[CF_3{\cdot}CH_2{\cdot}CHI{\cdot}Si{\cdot}O_{1.5}]_n$, $[CF_2Cl{\cdot}CFCl{\cdot}CH_2{\cdot}CHI{\cdot}Si{\cdot}O_{1.5}]_n$, and $[CF_2Cl{\cdot}CFCl{\cdot}CH_2{\cdot}CHI{\cdot}SiMe{\cdot}O]_n$ have been prepared; certain of them show good thermal stability. Reaction of an olefin with dichlorosilane provides a simple direct route to dialkyldichlorosilanes and thence the silicone. The unsaturated compounds $CF_2Br{\cdot}CH{:}CH{\cdot}SiMe_3$, $CF_2Cl{\cdot}CFCl{\cdot}CH{:}CH{\cdot}SiMe_3$, and $CF_2{:}CF{\cdot}CH{:}CH{\cdot}SiMe_3$, have been isolated. Polymerisation of the diene $CF_2{:}CF{\cdot}CH{:}CH_2$ to give a rubber is mainly 1 : 4-, but is accompanied by 1 : 2-polymerisation involving only the $CH{:}CH_2$ group; polymerisation of $CF_2{:}CF{\cdot}CH{:}CH{\cdot}SiMe_3$ occurs similarly.

The first paper [1] in this series summarised the methods developed for the synthesis of polyfluoroalkyl compounds of silicon. Two of the main methods are exemplified in the present communication: (*a*) reaction of a compound containing an Si–H bond with a fluoro-olefin, (*b*) reaction of a polyfluoroalkyl iodide or bromide with an alkenylsilicon compound. Both involve free radicals as intermediates.

3 : 3 : 3-Trifluoropropene reacts smoothly with trichlorosilane on exposure to ultraviolet light:

$$SiHCl_3 \xrightarrow{h\nu} {\cdot}SiCl_3 + H{\cdot}$$

$${\cdot}SiCl_3 + CF_3{\cdot}CH{:}CH_2 \longrightarrow CF_3{\cdot}\dot{C}H{\cdot}CH_2{\cdot}SiCl_3$$

$$CF_3{\cdot}\dot{C}H{\cdot}CH_2{\cdot}SiCl_3 + SiHCl_3 \longrightarrow CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}SiCl_3 + {\cdot}SiCl_3 \text{ (Chain transfer)}$$

(I)

Unlike the reaction between tetrafluoroethylene and trichlorosilane,[1] there is no need to use a large excess of the chain-transfer agent to obtain good yields of the 1 : 1 adduct, since trifluoropropene polymerises with itself only with difficulty. There was no indication of the formation of material of b. p. higher than that of the 1 : 1 adduct even when approximately equimolar quantities of reactants were used.

The 1 : 1 adduct (91% yield) is assigned structure (I) rather than the alternative $CH_2I{\cdot}CH(CF_3){\cdot}SiCl_3$, since earlier studies [2] have shown that free radicals attack the CH_2 group of compounds $R{\cdot}CH{:}CH_2$ exclusively no matter what the nature of R. Proof of structure is afforded by the synthesis of compound (I) from 3 : 3 : 3-trifluoropropylmagnesium iodide and silicon tetrachloride. Presence of three fluorine atoms decreases the b. p. by approximately 10° relative to trichloro-*n*-propylsilane. The trichloro-compound (I) rapidly yields the trimethoxy-compound (II) with methanol. Aqueous hydrolysis affords the white solid polysiloxane (III).

* Part III, *J.*, 1957, 3925.

† Presented in part at the Amer. Chem. Soc. Meeting, Minneapolis, 1955, Abstracts, p. 43M.

[1] Haszeldine and Marklow, *J.*, 1956, 962.

[2] Haszeldine and Steele, *J.*, 1955, 3005, and preceding papers; Haszeldine, *J.*, 1952, 2504.

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The polyfluoroalkylsilicone (IV) was synthesised in good yield by photochemical addition of methyldichlorosilane to 3 : 3 : 3-trifluoropropene to give methyl-3 : 3 : 3-trifluoropropyldichlorosilane (V), followed by aqueous hydrolysis. Replacement of a chlorine in compound (I) by methyl raises the b. p. by approximately 10°. The dichloro-compound (V) with methanol gives the corresponding dimethoxy-compound which, when treated with water, also yielded silicone (IV).

$CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}Si(OMe)_3$ (II) $\quad$ $[CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}Si{\cdot}O_{1\cdot5}]_n$ (III) $\quad$ $[CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}SiMe{\cdot}O]_n$ (IV)

$CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}SiMeCl_2$ (V)

A second route to polyfluoroalkyl silicones with fluorine in the γ-position to silicon utilises dichlorosilane in the free-radical addition reactions:

$$SiH_2Cl_2 \xrightarrow{h\nu} {\cdot}SiHCl_2 + H{\cdot}$$

$${\cdot}SiHCl_2 + CF_3{\cdot}CH{:}CH_2 \longrightarrow CF_3{\cdot}\dot{C}H{\cdot}CH_2{\cdot}SiHCl_2 \xrightarrow{SiH_2Cl_2} CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}SiHCl_2 + {\cdot}SiHCl_2$$
(VI)

$$CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}SiHCl_2 \xrightarrow{h\nu} CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}SiCl_2{\cdot} + H{\cdot}$$

$$CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}SiCl_2{\cdot} + CF_3{\cdot}CH{:}CH_2 \longrightarrow CF_3{\cdot}\dot{C}H{\cdot}CH_2{\cdot}SiCl_2{\cdot}CH_2{\cdot}CH_2{\cdot}CF_3$$

$$\downarrow CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}SiHCl_2$$

(VII) $(CF_3{\cdot}CH_2{\cdot}CH_2)_2SiCl_2 + CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}SiCl_2{\cdot}$

$$(CF_3{\cdot}CH_2{\cdot}CH_2)_2SiCl_2 \xrightarrow{H_2O} [(CF_3{\cdot}CH_2{\cdot}CH_2)_2Si{\cdot}O]_n \quad \text{(VIII)}$$

This route is particularly useful with olefins such as 3 : 3 : 3-trifluoropropene since chain propagation to give $CF_3{\cdot}CH(CH_2{\cdot}CH_2{\cdot}CF_3){\cdot}CH_2{\cdot}SiHCl_2$ does not occur. The 1 : 1 adduct (VI) contains an Si–H bond and, unless an excess of dichlorosilane is used as chain-transfer agent, a secondary reaction sets in whereby the product (VI) reacts with more trifluoropropene to give dichlorodi-(3 : 3 : 3-trifluoropropyl)silane (VII). Isolation of the product (VI) in good yield thus requires an excess of dichlorosilane. If only the precursor (VII) of the silicone (VIII) is required, however, it is readily obtained by reaction of dichlorosilane with an excess of trifluoropropene. Conversion of the dichloro-compound (VII) into the corresponding dimethoxy-compound followed by aqueous hydrolysis, or hydrolysis of the dichloro-compound itself, gives the silicone (VIII).

Silicones containing heptafluoropropyl or trifluoro*iso*propyl groups were similarly obtained:

$$C_3F_7{\cdot}CH{:}CH_2 + CH_3{\cdot}SiHCl_2 \xrightarrow{h\nu} C_3F_7{\cdot}CH_2{\cdot}CH_2{\cdot}SiMeCl_2$$

$$\downarrow EtOH \qquad \xrightarrow{H_2O} [C_3F_7{\cdot}CH_2{\cdot}CH_2{\cdot}SiMe{\cdot}O]_n$$

$$C_3F_7{\cdot}CH{:}CH_2 + CH_3{\cdot}SiH(OEt)_2 \xrightarrow{h\nu} C_3F_7{\cdot}CH_2{\cdot}CH_2{\cdot}SiMe(OEt)_2 \xrightarrow{H_2O}$$

$$CF_3{\cdot}CMe{:}CH_2 + CH_3{\cdot}SiHCl_2 \xrightarrow{h\nu} CF_3{\cdot}CHMe{\cdot}CH_2{\cdot}SiMeCl_2 \xrightarrow{H_2O} [CF_3{\cdot}CHMe{\cdot}CH_2{\cdot}SiMe{\cdot}O]_n$$

Both silicones were colourless viscous oils. That containing the trifluoro*iso*propyl group was partially volatile at 100—200°/10^{-1} mm., suggesting that cyclic siloxanes were present.

The monomers (I), (VII), $C_3F_7{\cdot}CH_2{\cdot}CH_2{\cdot}SiMeCl_2$, and $CF_3{\cdot}CHMe{\cdot}CH_2{\cdot}SiMeCl_2$, the

polysiloxane (III), and the silicones (IV), (VIII), and $[C_3F_7{\cdot}CH_2{\cdot}CH_2{\cdot}SiMe{\cdot}O]_n$ are stable at 250° and break down only slowly at 300°.

The second general method used for the synthesis of polyfluoroalkylsilicon compounds involves free-radical addition of polyhalogenoalkyl iodides or bromides, *e.g.*, CF_3I, CF_2Br_2, $CF_2Cl{\cdot}CFClI$, or CCl_3Br, to alkenylsilanes, *e.g.*, $CH_2{:}CH{\cdot}SiX_3$ (X = Cl or alkyl). The reaction follows the general scheme:

$$CF_3I \xrightarrow{h\nu} CF_3{\cdot} + I{\cdot}$$

$$CF_3{\cdot} + CH_2{:}CH{\cdot}SiX_3 \longrightarrow CF_3{\cdot}CH_2{\cdot}\dot{C}H{\cdot}SiX_3 \xrightarrow{CF_3I} CF_3{\cdot}CH_2{\cdot}CHI{\cdot}SiX_3$$

The direction of free-radical attack on the vinylsilane can be predicted with certainty from earlier studies.[2] Vinylsilanes do not homopolymerise *via* the ethylenic link readily, and the chain propagation reaction

$$CF_3{\cdot}CH_2{\cdot}\dot{C}H{\cdot}SiX_3 + CH_2{:}CH{\cdot}SiX_3 \longrightarrow CF_3{\cdot}CH_2{\cdot}CH(SiX_3){\cdot}CH_2{\cdot}\dot{C}H{\cdot}SiX_3$$

is thus insignificant, with consequent high yields of 1 : 1 adducts. The compounds so prepared are shown in the annexed Table.

Polyhalogenoalkane	Vinylsilane	1 : 1 Adduct
CF_3I	$CH_2{:}CH{\cdot}SiMe_3$	$CF_3{\cdot}CH_2{\cdot}CHI{\cdot}SiMe_3$ (IX)
CF_2Br_2	,,	$CF_2Br{\cdot}CH_2{\cdot}CHBr{\cdot}SiMe_3$ (X)
$CF_2Cl{\cdot}CFClI$	,,	$CF_2Cl{\cdot}CFCl{\cdot}CH_2{\cdot}CHI{\cdot}SiMe_3$ (XI)
CF_3I	$CH_2{:}CH{\cdot}SiCl_3$	$CF_3{\cdot}CH_2{\cdot}CHI{\cdot}SiCl_3$ (XII)
$CF_2Cl{\cdot}CFClI$	,,	$CF_2Cl{\cdot}CFCl{\cdot}CH_2{\cdot}CHI{\cdot}SiCl_3$ (XIII)
CCl_3Br	,,	$CCl_3{\cdot}CH_2{\cdot}CHBr{\cdot}SiCl_3$ (XIV)
$CF_2Cl{\cdot}CFClI$	$CH_2{:}CH{\cdot}SiMeCl_2$	$CF_2Cl{\cdot}CFCl{\cdot}CH_2{\cdot}CHI{\cdot}SiMeCl_2$ (XV)

Dehydroiodination of trimethyl-(3 : 3 : 3-trifluoro-1-iodopropyl)silane (IX) by hot quinoline gave the trifluoropropenylsilane but not analytically pure. Dehydrobromination of 1 : 3-dibromo-3 : 3-difluoropropyltrimethylsilane (X) gave, however, the pure propenylsilane $CF_2Br{\cdot}CH{:}CH{\cdot}SiMe_3$. Ethanolic potassium hydroxide removed hydrogen iodide from the adduct (XI) to give the olefin $CF_2Cl{\cdot}CFCl{\cdot}CH{:}CH{\cdot}SiMe_3$, and mild treatment of this in ether with zinc gave trimethyl-(3 : 4 : 4-trifluorobuta-1 : 3-dienyl)silane (XVI). In presence of acetyl peroxide this compound readily gave a polymer containing both $-CF_2{\cdot}CF{:}CH{\cdot}CH-$ and $CF_2{:}CF-$ units as shown by C:C infrared absorption at 5·80 and 5·57 μ, respectively:

$$\underset{\text{(XVI)}}{CF_2{:}CF{\cdot}CH{:}CH{\cdot}SiMe_3} \xrightarrow{Ac_2O} [-CF_2{\cdot}CF{:}CH{\cdot}\underset{\displaystyle SiMe_3}{\underset{|}{CH}}-]_n-[-\underset{\displaystyle CF{:}CF_2}{\underset{|}{CH}}-\underset{\displaystyle SiMe_3}{\underset{|}{CH}}-]_m$$

Polymerisation has thus involved both 1 : 4- and 1 : 2- (on the $-CH{:}CH-$ group) addition, but not 3 : 4-addition, since there was no indication of the presence of a $CH{:}CH-$ band in the spectrum.

Trichloro-(3 : 3 : 3-trifluoro-1-iodopropyl)silane (XII) showed C–I absorption at 275 mμ in light petroleum, and the related compound $CF_3{\cdot}CH_2{\cdot}CHI{\cdot}Si(OEt)_3$ showed maximum absorption at 267 mμ in ethanol. There is thus a shift of the peak to the red compared with a secondary iodide such as *iso*propyl iodide [3] ($\lambda_{max.}$ 261 mμ in light petroleum and in ethanol), or 1 : 1 : 1-trifluoro-3-iodobutane [4] ($\lambda_{max.}$ 264 mμ in ethanol), associated with the presence of silicon α to the >CHI group. The trichloro-compound (XII) is hydrolysed to the glass-like polysiloxane $[CF_3{\cdot}CH_2{\cdot}CHI{\cdot}Si{\cdot}O_{1\cdot5}]_n$ which also shows C–I absorption in ethanol at 267 mμ. Reaction of this polysiloxane with dilute aqueous alkali gave the unsaturated polysiloxane $[CF_2{\cdot}CH{:}CH{\cdot}Si{\cdot}O_{1\cdot5}]_n$ but not analytically pure.

Attempts to deiodochlorinate trichloro-(3: 3 : 3-trifluoro-1-iodopropyl)silane (XII) to

[3] Haszeldine, *J.*, 1953, 1764.
[4] Haszeldine, Leedham, and Steele, *J.*, 1954, 2040.

give the compound $CF_3{\cdot}CH_2{\cdot}CH{:}SiCl_2$ led only to iodine-free material of high molecular weight, suggesting that the monomer, if produced at all, soon polymerised. Trichloro-(3 : 4-dichloro-3 : 4 : 4-trifluoro-1-iodobutyl)silane (XIII) was produced only slowly photochemically, probably because both reactants had only a low vapour pressure. It, and its triethoxy-analogue, showed ultraviolet absorption in light petroleum or ethanol typical of the $-CX_2{\cdot}CH_2{\cdot}CHI{\cdot}Si\leqslant$ system. Aqueous sodium hydroxide at 100° converted the pentachloride (XIII) into 3 : 4-dichloro-3 : 4 : 4-trifluorobutene and silicate. Hydrolytic carbon–silicon fission thus occurs, somewhat surprisingly, even when the fluorine is as far removed as the γ-carbon atom and with only a weakly electronegative element such as iodine on the α-carbon atom. If $CF_2Cl{\cdot}CFCl{\cdot}CH_2{\cdot}CH_2I$, which can also be obtained by photochemical reaction of 1 : 2-dichloro-1 : 2 : 2-trifluoro-1-iodoethane with ethylene, were the intermediate hydrolysis product, it would be dehydroiodinated by the aqueous base to give the butene. Alternatively, initial dehydroiodination to $CF_2Cl{\cdot}CFCl{\cdot}CH{:}CH{\cdot}Si\leqslant$ would enable the inductive effect of the $CF_2Cl{\cdot}CFCl-$ group to be relayed to the silicon, so promoting nucleophilic attack on that atom.[1] Aqueous hydrolysis of the halide (XIII) yields the polysiloxane, which also shows C–I absorption in ethanolic solution. The polysiloxane is also cleaved hydrolytically by aqueous base at 100° to give 3 : 4-dichloro-3 : 4 : 4-trifluorobutene.

This olefin shows the C:C stretching vibration as a weak band at 6·03 μ, the position typical of a polyfluoroalkylethylene of type $R{\cdot}CH{:}CH_2$. The out-of-plane C–H vibrations are at 10·19 and 10·38 μ (cf. 10·10, 10·99 μ when R is a hydrocarbon group). Zinc and ether dechlorinate the olefin to the diene $CF_2{:}CF{\cdot}CH{:}CH_2$. This readily polymerises, and study of the infrared spectra of the polymers shows that both 1 : 2- and (predominantly) 1 : 4-addition occur. It was pointed out earlier [5] that perfluorobutadiene behaves in some ways as if conjugation between the double bonds was poor, *i.e.*, as if the double bonds were isolated. Of the two types of double bond in 1 : 1 : 2-trifluorobuta-1 : 3-diene, the $-CH{:}CH_2$ type will certainly be more sensitive to free-radical attack than the $-CF{:}CF_2$ type.[2] It is not unexpected therefore to find a band in the infrared spectrum of the polymer produced with acetyl peroxide at 5·58 μ typical of the $-CF{:}CF_2$ group, *i.e.*, polymerisation involving 1 : 2-addition occurs in part:

$$CF_2{:}CF{\cdot}CH{:}CH_2 \xrightarrow{Ac_2O_2} -CH_2-\underset{\displaystyle CF{:}CF_2}{CH}-CH_2-\underset{\displaystyle CF{:}CF_2}{CH}-$$

There is no band in the region typical of $-CH{:}CH_2$ group absorption, *i.e.*, 1 : 2-polymerisation involving the $-CF{:}CF_2$ group does not occur. The main C:C band is at 5·80 μ, typical of the $-CF_2{\cdot}CF{:}CH{\cdot}CH_2-$ group produced by 1 : 4-polymerisation:

$$CH_2{:}CH{\cdot}CF{:}CF_2 \xrightarrow{Ac_2O_2} -CH_2{\cdot}CH{:}CF{\cdot}CF_2{\cdot}CH_2{\cdot}CH{:}CF{\cdot}CF_2-$$

Benzoyl peroxide converts the diene into a polymer containing mainly $-CH_2{\cdot}CH{:}CF{\cdot}CF_2-$ units. The double bonds in the diene thus show appreciable, though incomplete, conjugation.

1 : 2-Dichloro-1 : 2 : 2-trifluoro-1-iodoethane reacted readily with dichloromethylvinylsilane to give the 1 : 1 adduct (XV) which, on aqueous hydrolysis, gave the silicone $[CF_2Cl{\cdot}CFCl{\cdot}CH_2{\cdot}CHI{\cdot}SiMe{\cdot}O]_n$.

The polysiloxane $[CCl_3{\cdot}CH_2{\cdot}CHBr{\cdot}Si{\cdot}O_{1\cdot5}]_n$, obtained by aqueous hydrolysis of (1-bromo-3 : 3 : 3-trichloropropyl)trichlorosilane (XIV), contains a terminal CCl_3 group; when this was treated with concentrated sulphuric acid hydrolysis occurred to give the polysiloxane $[HO_2C{\cdot}CH_2{\cdot}CHBr{\cdot}Si{\cdot}O_{1\cdot5}]_n$.

The above results show that the free-radical addition approach for the synthesis of polyfluoroalkyl silicon compounds is convenient and sufficiently versatile to enable

[5] Haszeldine, *J.*, 1952, 4423.

silicones and polysiloxanes to be prepared with the fluorine atoms attached to carbon in the α- or γ-position relative to silicon. The site of the fluorine has a profound influence on the thermal and hydrolytic stability of such compounds, as will be shown in a later paper.

Experimental

Reactions were carried out in sealed tubes which were filled by use of a conventional apparatus for manipulation of volatile compounds. Air and moisture were thus excluded, and the tubes were sealed *in vacuo*.

Reaction of **3 : 3 : 3-***Trifluoropropene with Trichlorosilane.*—The olefin (60 mmoles) and trichlorosilane (62 mmoles), sealed in a 200-ml. silica tube and shaken whilst exposed to ultraviolet light for 96 hr., gave unchanged olefin (5%), trichlorosilane (6%), and *trichloro-*(**3 : 3 : 3-***trifluoropropyl*)*silane* (91%) (Found: C, 15·6; H, 1·6. $C_3H_4Cl_3F_3Si$ requires C, 15·6; H, 1·7%), b. p. 113°.

This silane (1·1 g.), added dropwise to an excess of anhydrous methanol (4 ml.), then shaken for 1 hr., gave, on distillation, *trimethoxy-*(**3 : 3 : 3-***trifluoropropyl*)*silane* (79%) (Found: C, 33·1; H, 6·1. $C_6H_{13}O_3F_3Si$ requires C, 33·0; H, 6·0%), b. p. 144°/760 mm., 84°/90 mm.

An ethereal solution of trichloro-(3 : 3 : 3-trifluoropropyl)silane (2·1 g. in 10 ml.) was shaken with water (10 ml.) for 30 min. The ether was evaporated at room temperature from the dried (Na_2SO_4) extract to give the *polysiloxane* $[CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}SiO_{1.5}]_n$ (93%) (Found: C, 24·0; H, 2·9. $C_3H_4O_{1.5}F_3Si$ requires C, 24·2; H, 2·7%) as a white, free-running solid.

Reaction of ethereal 3 : 3 : 3-trifluoropropylmagnesium iodide (0·16 mole) with silicon tetrachloride (0·51 mole) at 20—30° for 24 hr. gave trichloro-(3 : 3 : 3-trifluoropropyl)silane, b. p. 113—114°, in 23% yield.

Reaction of **3 : 3 : 3-***Trifluoropropene with Methyldichlorosilane.*—The olefin (53 mmoles) and methyldichlorosilane (55 mmoles), exposed to ultraviolet light in a sealed 200-ml. silica tube for 82 hr., gave *methyl-***3 : 3 : 3-***trifluoropropyldichlorosilane* (92%) (Found: C, 22·8; H, 3·2. $C_4H_7Cl_2F_3Si$ requires C, 22·8; H, 3·3%), b. p. 125°. No unchanged olefin was detected.

Methyl-3 : 3 : 3-trifluoropropyldichlorosilane (1·7 g.), added slowly with shaking to anhydrous methanol, gave *dimethoxy-methyl-***3 : 3 : 3-***trifluoropropylsilane* (71%) (Found: C, 35·4; H, 6·4. $C_6H_{13}O_2F_3Si$ requires C, 35·6; H, 6·4%), b. p. 85°/150 mm., 100°/283 mm.

Methyl-3 : 3 : 3-trifluoropropyldichlorosilane (3·1 g.) was added slowly to a stirred mixture of ether (10 ml.) and water (10 ml.). The ethereal extract was dried (Na_2SO_4) and removal of the ether on a water-bath left the *silicone* $[(CF_3{\cdot}CH_2{\cdot}CH_2)(CH_3)Si{\cdot}O]_n$ (90%) (Found: C, 30·7; H, 4·4. $C_4H_7OF_3Si$ requires C, 30·8; H, 4·5%) as a clear, colourless, viscous oil. A similar viscous silicone was obtained by aqueous hydrolysis of the dimethoxy-compound.

Reaction of **3 : 3 : 3-***Trifluoropropene with Dichlorosilane.*—The olefin (40 mmoles) and dichlorosilane (100 mmoles) were sealed in a 200-ml. silica tube and exposed to ultraviolet light for 64 hr. Distillation *in vacuo* gave unchanged dichlorosilane (51%), unchanged olefin (3%), trichlorosilane (2%), *dichloro-***3 : 3 : 3-***trifluoropropylsilane* (83%) (Found: C, 18·2; H, 2·4. $C_3H_5Cl_2F_3Si$ requires C, 18·3; H, 2·5%), b. p. 90—91°, and a small amount of liquid of higher b. p., probably $(CF_3{\cdot}CH_2{\cdot}CH_2)_2SiCl_2$ (see below).

Dichloro-3 : 3 : 3-trifluoropropylsilane (70 mmoles; prepared as above) and 3 : 3 : 3-trifluoropropene (65 mmoles), irradiated for 80 hr. in a silica tube, gave unchanged reactants (8%) and *dichlorodi-*(**3 : 3 : 3-***trifluoropropyl*)*silane* (85%) (Found: C, 24·4; H, 2·5. $C_6H_8Cl_2F_6Si$ requires C, 24·6; H, 2·7%), b. p. 162—163°.

Dichlorosilane (35 mmoles) and 3 : 3 : 3-trifluoropropene (102 mmoles), irradiated for 107 hr. in a silica tube, gave unchanged olefin, dichloro-3 : 3 : 3-trifluoropropylsilane (9%), and dichlorodi-(3 : 3 : 3-trifluoropropyl)silane (77%), b. p. 162—163°. Yields are based on dichlorosilane.

Reaction of dichlorodi-(3 : 3 : 3-trifluoropropyl)silane (2·9 g.) with a 10% excess of anhydrous methanol gave *dimethoxydi-*(**3 : 3 : 3-***trifluoropropyl*)*silane* (88%) (Found: C, 33·5; H, 4·9. $C_8H_{14}O_2F_6Si$ requires C, 33·8; H, 4·9%), b. p. 175—176°/760 mm., 96°/60 mm.

To dichlorodi-(3 : 3 : 3-trifluoropropyl)silane (2·7 g.) and ether (5 ml.) was slowly added a saturated solution of water in ether (20 ml.). The solution was then poured with stirring into an excess of water (10 ml.). Removal of the ether from the dried ethereal extract gave the *silicone* $[(CF_3{\cdot}CH_2{\cdot}CH_2)_2Si{\cdot}O]_n$ (91%) (Found: C, 30·1; H, 3·5. $C_6H_8OF_6Si$ requires C, 30·3; H, 3·4%) as a colourless oil with negligible volatility at 200°. A similar oil was obtained by aqueous hydrolysis of the ethereal dimethoxy-compound.

XUM

Reaction of **3 : 3 : 4 : 4 : 5 : 5 : 5-***Heptafluoropentene with Methyldichlorosilane or Methyldiethoxysilane.*—The olefin (50 mmoles) and methyldichlorosilane (60 mmoles) were sealed in a 200-ml. silica tube which was shaken vigorously whilst horizontal so as to disperse the reactants as a liquid film over the whole surface of the tube. Smooth reaction ensued on irradiation and after 88 hr. distillation gave *dichloro*-**3 : 3 : 4 : 4 : 5 : 5 : 5-***heptafluoropentylmethylsilane* (73%) (Found: C, 23·0; H, 2·1. $C_6H_7Cl_2F_7Si$ requires C, 23·2; H, 2·3%), b. p. 72°/70 mm., 147°/760 mm.

A portion of this product (1·8 g.) in ether (5 ml.) was added slowly to a stirred mixture of water (5 ml.) and ether (10 ml.). Removal of the ether from the dried ethereal extracts left the *silicone* $[C_3F_7{\cdot}CH_2{\cdot}CH_2{\cdot}SiMe{\cdot}O]_n$ (87%) (Found: C, 27·9; H, 2·7. $C_6H_7OF_7Si$ requires C, 28·1; H, 2·7%) as a colourless viscous liquid.

To a second portion of dichloro-**3 : 3 : 4 : 4 : 5 : 5 : 5**-heptafluoropentylmethylsilane (3·2 g.) was added a 10% excess of anhydrous ethanol. After being heated at 50° for 2 hr. the solution was distilled to give *diethoxy*-**3 : 3 : 4 : 4 : 5 : 5 : 5-***heptafluoropentylmethylsilane* (67%) (Found: C, 36·4; H, 5·2. $C_{10}H_{17}O_2F_7Si$ requires C, 36·6; H, 5·2%), b. p. 82—83°/28 mm. Addition of water to a shaken ethereal solution of the diethoxy-compound and removal of ether from the dried ethereal extract gave the silicone $[C_3F_7{\cdot}CH_2{\cdot}CH_2{\cdot}SiMe{\cdot}O]_n$ (91%) (Found: C, 28·0; H, 2·6%).

Methyldiethoxysilane (30 mmoles) and **3 : 3 : 4 : 4 : 5 : 5 : 5**-heptafluoropentene (30 mmoles), shaken and exposed to ultraviolet light for 3 days, gave diethoxy-**3 : 3 : 4 : 4 : 5 : 5 : 5**-heptafluoropentylmethylsilane (79%) (Found: C, 36·6; H, 5·0%), b. p. 82—84°/28 mm., identical with the material described above.

Reaction of **3 : 3 : 3-***Trifluoro-2-methylpropene with Methyldichlorosilane.*—**3 : 3 : 3**-Trifluoro-2-methylpropene (56 mmoles) and methyldichlorosilane (61 mmoles) in a 200-ml. silica tube were shaken and exposed to ultraviolet light for 98 hr. Distillation gave *methyl*-(**3 : 3 : 3-***trifluoro-2-methylpropyl*)*dichlorosilane* (63%) (Found: C, 26·5; H, 4·1. $C_5H_9Cl_2F_3Si$ requires C, 26·7; H, 4·0%), b. p. 139°.

To a stirred solution of the dichloro-compound (2·6 g.) in ether (8 ml.) was slowly added wet ether (10 ml.), then water (5 ml.) dropwise. Removal of ether from the dried ethereal extract gave the *silicone* $[CF_3{\cdot}CHMe{\cdot}CH_2{\cdot}SiMe{\cdot}O]_n$ (Found: C, 35·0; H, 5·4. $C_5H_9OF_3Si$ requires C, 35·3; H, 5·3%) as a mobile oil. Approximately 10% of the oil distilled when it was heated from 100° to 200°/10^{-1} mm. in a short-path still, indicating the presence of cyclic polysiloxanes.

Thermal Stability of Certain Fluoroalkylsilicon Compounds.—Preliminary information was obtained about thermal stability by heating samples (1·0—1·5 g.) in 20-ml., sealed, evacuated, silica tubes for 24 hr. The compounds $CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}SiCl_3$, $(CF_3{\cdot}CH_2{\cdot}CH_2)_2SiCl_2$, $C_3F_7{\cdot}CH_2{\cdot}CH_2{\cdot}SiMeCl_2$, and $CF_3{\cdot}CHMe{\cdot}CH_2{\cdot}SiMeCl_2$ failed to give volatile breakdown products at 200° or 250°, and were partially decomposed (15—20%) at 300° after 6 hr. The polysiloxane, $[CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}Si{\cdot}O_{1\cdot5}]_n$, and the silicones, $[CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}SiMe{\cdot}O]_n$, $[(CF_3{\cdot}CH_2{\cdot}CH_2)_3Si{\cdot}O]_n$, and $[C_3F_7{\cdot}CH_2{\cdot}CH_2{\cdot}SiMe{\cdot}O]_n$, were unaffected at 250° and gave only a low yield (10—15%) of volatile product after 6 hr. at 300°.

Reaction of Vinyltrimethylsilane with Trifluoroiodomethane.—The olefin (75 mmoles) and trifluoroiodomethane (67 mmoles), sealed in a 200-ml. silica tube and shaken whilst exposed to ultraviolet light for 102 hr., gave unchanged olefin (12%), only a trace of trifluoroiodomethane, and *trimethyl*-(**3 : 3 : 3-***trifluoro-1-iodopropyl*)*silane* (79%) (Found: C, 24·3; H, 4·2. $C_6H_{12}F_3ISi$ requires C, 24·3; H, 4·1%), b. p. 72°/20 mm.

Dehydroiodination occurred when the compound (2·1 g.) was heated to 120° with quinoline, but final purification of the trimethyltrifluoropropenylsilane (Found: *M*, 162. Calc. for $C_6H_{11}F_3Si$: *M*, 168) could not be effected on the scale used.

Reaction of Vinyltrimethylsilane with Dibromodifluoromethane.—The bromo-compound (69 mmoles) and the olefin (70 mmoles), irradiated in a 200-ml. silica tube for 120 hr., gave unchanged olefin (23%) and dibromodifluoromethane (21%) and **1 : 3-***dibromo*-**3 : 3-***difluoropropyltrimethylsilane* (79% based on bromo-compound consumed) (Found: C, 23·0; H, 4·1. $C_6H_{12}Br_2F_2Si$ requires C, 23·2; H, 3·9%), b. p. 95°/25 mm.

Reaction of this product (4·1 g.) with quinoline (8 g.) at 120° in a sealed tube for 10 hr. gave unchanged starting material (37%) and **3-***bromo*-**3 : 3-***difluoropropenyltrimethylsilane* (48% based on starting material consumed) (Found: C, 31·8; H, 4·8. $C_6H_{11}BrF_2Si$ requires C, 31·5; H, 4·8%), b. p. 66—68°/52 mm. The compound gave a dibromide when exposed to ultraviolet light with bromine for 30 min.

Reaction of Vinyltrimethylsilane with 1 : 2-*Dichloro*-1-*iodotrifluoroethane*.—The same quantities and conditions were used as for the dibromodifluoromethane reaction above. Distillation gave unchanged olefin (10%) and 3 : 4-*dichloro*-3 : 4 : 4-*trifluoro*-1-*iodobutyltrimethylsilane* (66%) (Found: C, 22·1; H, 3·2. $C_7H_{12}Cl_2F_3ISi$ requires C, 22·2; H, 3·2%), b. p. 99—100°/9 mm.

To this compound (3·9 g.), dissolved in ethanol (5 ml.), was added dropwise with stirring a 10% excess of 10% ethanolic potassium hydroxide at 0° during 3 hr. Addition of an excess of water (400 ml.), separation of the lower layer, drying, and distillation gave 3 : 4-*dichloro*-3 : 4 : 4-*trifluorobutenyltrimethylsilane* (57%) (Found: C, 33·3; H, 4·5. $C_7H_{11}Cl_2F_3Si$ requires C, 33·5; H, 4·4%), b. p. 57—59°/15 mm. The presence of the double bond was confirmed by the rapid absorption of chlorine at room temperature in the dark.

3 : 4-Dichloro-3 : 4 : 4-trifluorobutenyltrimethylsilane (4·4 g.) in ether (5 ml.) was added dropwise to powdered zinc (4 g.) and ether (25 ml.) at 50°. Dehalogenation was complete after 4 hr. and treatment of the filtered solution with an excess of water, followed by distillation of the organic layer, gave *trimethyl*-(3 : 4 : 4-*trifluorobuta*-1 : 3-*dienyl*)*silane* (31%) (Found: C, 46·3; H, 6·0. $C_7H_{11}F_3Si$ requires C, 46·6; H, 6·1%), b. p. 25°/25 mm., approx. 110—113°/760 mm. When this was heated to 100° in a sealed tube with a small amount of acetyl peroxide, polymerisation occurred to give a white, stable solid showing $-CF{:}CF_2$ absorption at 5·57 μ, stronger $-CF_2{\cdot}CH{:}CF{\cdot}CH-$ absorption at 5·80 μ, and no band in the $-CH{:}CH-$ region (5·9—6·3 μ).

Reaction of Trifluoroiodomethane with Vinyltrichlorosilane.—The iodo-compound (22 mmoles) and vinyltrichlorosilane (27·5 mmoles) in a 200-ml. silica tube were irradiated for 9·5 days. Distillation gave unchanged reactants and *trichloro*-(3 : 3 : 3-*trifluoro*-1-*iodopropyl*)*silane* (35%) (Found: C, 10·1; H, 0·9; Si, 7·7. $C_3H_2Cl_3F_3ISi$ requires C, 10·1; H, 0·8; Si, 7·9%), b. p. 79°/25 mm. Ultraviolet absorption:

Solvent	$\lambda_{max.}$	ε	$\lambda_{min.}$	ε
Light petroleum	275	400	228	60
Dioxan	265	530	231	160
EtOH *	267	430	226	90

* Reacts with solute to give $CF_3{\cdot}CH_2{\cdot}CHI{\cdot}Si(OEt)_3$.

Trichloro-(3 : 3 : 3-trifluoro-1-iodopropyl)silane (2·27 mmoles), shaken with water (50 ml.) and ether (50 ml.), gave, on evaporation of the dried ethereal extract, the *polysiloxane* $[CF_3{\cdot}CH_2{\cdot}CHI{\cdot}Si{\cdot}O_{1\cdot5}]_n$ (88%) (Found: C, 13·1; H, 1·5. $C_3H_2F_3ISiO_{1\cdot5}$ requires C, 13·1; H, 1·1%) as a colourless glass. Ultraviolet absorption in EtOH: $\lambda_{max.}$ 267 (ε 420), $\lambda_{min.}$ 232 (ε 135).

The polysiloxane (0·8 mmole) was shaken with 2% aqueous sodium hydroxide (15 ml.) for 10 min., then kept overnight at 20°. The aqueous solution gave a strong positive test for iodide. There were no volatile products. Acidification and extraction with ether (50 ml.) gave a white powder, m. p. >250°, probably the polysiloxane $[CF_3{\cdot}CH{:}CH{\cdot}Si{\cdot}O_{1\cdot5}]_n$ but not analytically pure.

Trichloro-(3 : 3 : 3-trifluoro-1-iodopropyl)silane (3·48 mmoles), anhydrous tetrahydrofuran (3 ml.), and zinc powder (0·6 g.) were shaken in a sealed tube at 75° for 14 hr. Only polymeric material was isolated from the organic phase after removal of solid products by centrifuging. The iodo-compound (4·35 mmoles) failed to react with zinc in presence of light petroleum during 15 hr. at 20°. The iodo-compound (4·25 mmoles), zinc (0·73 g.), and anhydrous ether (4 ml.), shaken at 20° for 12 hr. in a sealed tube, gave only polymer on examination of the ethereal phase.

Reaction of 1 : 2-*Dichloro*-1-*iodotrifluoroethane with Vinyltrichloro*)*silane*.—The iodo-compound (75 mmoles) and vinyltrichlorosilane (41 mmoles), exposed to ultraviolet light for 9 days, gave unchanged reactants and *trichloro*-(3 : 4-*dichloro*-3 : 4 : 4-*trifluoro*-1-*iodobutyl*)*silane* (26%) (Found: C, 10·9; H, 0·7. $C_4H_3Cl_5F_3ISi$ requires C, 10·9; H, 0·7%), b. p. 124°/*ca.* 1 mm. Ultraviolet spectra:

Solvent	$\lambda_{max.}$	ε	$\lambda_{min.}$	ε
Light petroleum	275·5	400	231	100
Dioxan	264	485	231	140
EtOH *	267·5	440	223	50

* Reacts with solute to give $CF_2Cl{\cdot}CFCl{\cdot}CH_2{\cdot}CHI{\cdot}Si(OEt)_3$.

XUM

Trichloro-(3 : 4-dichloro-3 : 4 : 4-trifluoro-1-iodobutyl)silane (1·43 mmoles) and 10% aqueous sodium hydroxide (20 ml.), heated at 100° (6 hr.), gave 3 : 4-*dichloro*-3 : 4 : 4-*trifluorobutene* (58%) (Found: C, 27·1; H, 1·9%; *M*, 179. $C_4H_3Cl_2F_3$ requires C, 26·8; H, 1·7%; *M*, 179), b. p. 79° (isoteniscope).

Hydrolysis by shaking a solution of the iodo-compound (3·57 mmoles) in ether (50 ml.) with water (50 ml.) for 1 hr. gave, on removal of the ether, the impure polysiloxane $[CF_2Cl{\cdot}CFCl{\cdot}CH_2{\cdot}CHI{\cdot}Si{\cdot}O_{1\cdot5})_n$, m. p. 48°, which could not be purified to give satisfactory analytical figures. Absorption spectrum in EtOH: $\lambda_{max.}$ 268 (ε 395), $\lambda_{min.}$ 233 (ε 165). Hydrolysis of the polysiloxane with 10% aqueous sodium hydroxide at 100° gave 3 : 4-dichloro-3 : 4 : 4-trifluorobutene (50%), identified by means of its infrared spectrum.

Polymerisation of 1 : 1 : 2-*Trifluorobuta*-1 : 3-*diene*.—3 : 4-Dichloro-3 : 4 : 4-trifluorobutene (30 mmoles) in dry ether (10 ml.) was added dropwise to zinc dust (4 g.) and refluxing ether (20 ml.) during 6 hr. The volatile product, removed through a reflux condenser kept at 10°, was transferred to an apparatus for manipulation of volatile compounds and distilled to give 1 : 1 : 2-trifluorobuta-1 : 3-diene (61%) (Found: *M*, 108. Calc. for $C_4H_3F_3$: *M*, 108), b. p. 8° (isoteniscope). Tarrant and Lilyquist [6] report b. p. 7·8° for this compound.

The diene (1·1 g.) and acetyl peroxide (5 mg.), heated in an evacuated, sealed, silica tube at 100° for 2 hr., gave a white rubber which was dissolved in chloroform and washed with dilute aqueous sodium hydroxide to remove traces of acetic acid, etc. The gum-rubber obtained on evaporation of the chloroform solution hardened if kept in air. A sample of the gum-rubber was softened by chloroform until it could be pressed into a thin film between two sodium chloride plates. Examination of its infrared spectrum revealed C:C band at 5·58 and 5·80 μ, with the former one-fifth of the intensity of the second. There was no absorption at 6·0—6·3 μ. A second elastomer was obtained from the diene (1·0 g.) and benzoyl peroxide (5 mg.) at 100° for 6 hr. This was swollen by, but did not dissolve in, chloroform. Examination of the infrared spectrum of a thin film of this polymer revealed a strong C:C band at 5·80, a weak band at 5·5—5·75, and absence of a band at 6·0—6·3 μ.

Reaction of Bromotrichloromethane with Vinyltrichlorosilane.—The bromo-compound (53 mmoles) and vinyltrichlorosilane (55 mmoles), sealed and shaken in a 200-ml. silica tube and exposed to ultraviolet light for 90 hr., gave (1-*bromo*-3 : 3 : 3-*trichloropropyl*)*trichlorosilane* (79%) (Found: C, 10·1; H, 0·9. $C_3H_3BrCl_6Si$ requires C, 10·0; H, 0·8%), b. p. 145°/35 mm. A solution of the product (1·3 g.) in ether (5 ml.) poured into stirred ice-water (10 ml.) gave, on evaporation of the dried ethereal solution, the *polysiloxane* $[CCl_3{\cdot}CH_2{\cdot}CHBr{\cdot}Si{\cdot}O_{1\cdot5}]_n$ (89%) (Found: C, 12·8; H, 1·2. $C_3H_3BrCl_3SiO_{1\cdot5}$ requires C, 13·0; H, 1·1%) as a white solid. The polysiloxane liberated hydrogen chloride when heated with concentrated sulphuric acid at 100°. After being washed with water the polysiloxane showed a distinct acid reaction and titration with alkali indicated the presence of $[HO_2C{\cdot}CH_2{\cdot}CHBr{\cdot}Si{\cdot}O_{1\cdot5}]_n$, although an analytically pure sample could not be obtained; infrared spectroscopic examination showed the presence of the carboxyl group by its broad absorption at 5·85 μ.

Reaction of 1 : 2-*Dichloro*-1-*iodotrifluoroethane with Methylvinyldichlorosilane*.—The iodo-compound (63 mmoles) and the olefin (65 mmoles) were exposed to ultraviolet light for 89 hr. to give unchanged olefin (27%) and *dichloro*-(3 : 4-*dichloro*-3 : 4 : 4-*trifluoro*-1-*iodobutyl*)*methylsilane* (58%) (Found: C, 14·1; H, 1·2. $C_5H_6Cl_4F_3ISi$ requires C, 14·3; H, 1·4%), b. p. 108°/25 mm. Hydrolysis of the product with water as described above gave the *silicone* $[CF_2Cl{\cdot}CFCl{\cdot}CH_2{\cdot}CHI{\cdot}SiMe{\cdot}O]_n$ (81%) (Found: C, 16·2; H, 1·6. $C_5H_6Cl_2F_3ISiO$ requires C, 16·4; H, 1·6%) as a colourless viscous liquid.

We are indebted to the Department of Scientific and Industrial Research for a Maintenance Allowance, 1954—1955 (to R. J. M.), and to the Société d'Electro-chimie, d'Electro-métallurgie et des Aciéries Electriques d'Ugine for leave of absence and financial support (A. M. G.).

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, May 29th*, 1957.]

[6] Tarrant and Lilyquist, *J. Amer. Chem. Soc.*, 1955, **77**, 3640.

XUM

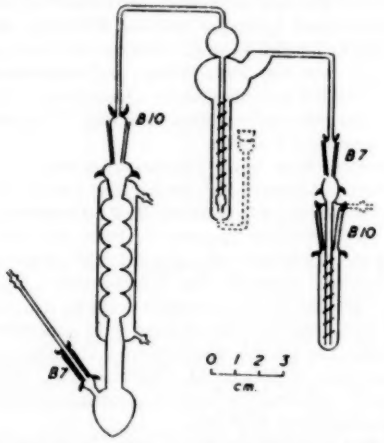
902. *Submicro-methods for the Analysis of Organic Compounds. Part II.* The Determination of Alkoxyl Groups.*

By R. Belcher, M. K. Bhatty, and T. S. West.

Alkoxyl groups can be determined on sample weights of the order of 50 μg. by suitable modification of Zeisel's method. Several sources of error have been eliminated. The results obtained are generally within ±0·3% absolute.

Zeisel's method [1] for determination of alkoxyl groups appeared to be adaptable to the submicro-scale. Vieböck and Brecher's modification,[2] in which the determination is completed iodometrically, was the most attractive because of the six-fold amplification of the titre; hence, before the design of suitable apparatus was attempted, preliminary trials were made to ensure that the titration could be successful at this level. Suitable amounts of standard iodate solution and, later, of standard iodide solution after oxidation to iodate by bromine water, were titrated; satisfactory results were obtained.

The size of the conventional micro-scale apparatus was reduced and several modifications were introduced.[3] The final form is shown in the Figure. The water-condenser



was shown to be essential. The main difficulty was the excessive " blank " values obtained on this scale of working; numerous details were studied, but these tests are not given, and it suffices to state that the following precautions must be taken: (1) The hydriodic acid must be prepared according to the instructions given later. (2) Nitrogen should be used as the carrier gas: carbon dioxide from the solid gave rise to high blanks owing to aerosol formation. (3) An efficient scrubber and scrubbing liquid must be used. The dimensions of the scrubber given in the Figure should be adhered to. The scrubbing liquid should be prepared fresh daily. (4) The rate of bubbling must be controlled carefully and should be about 1 bubble per second; a needle valve is essential for controlling the flow. (5) Irregular heating and draughts must be avoided. (6) Wherever rubber connections are used all the joints must be made glass-to-glass or metal-to-glass; if this precaution is not taken organic vapours in the atmosphere will penetrate the rubber and give rise to abnormal results. Aged rubber tubing must be used. (7) The apparatus must be kept clean; it

* Part I, *J.*, 1957, 4323.

[1] Zeisel, *Monatsh.*, 1885, **6**, 989.
[2] Vieböck and Brecher, *Ber.*, 1930, **63**, 3207.
[3] Bhatty, Ph.D. Thesis, Birmingham University, 1957.

should be dried in an oven which is free from the vapour of organic solvents after each determination. The value of the blanks should not exceed 10 μl. of 0·01N-sodium thiosulphate.

The results obtained in the determination of alkoxyl groups in ten organic compounds on sample weights of 45—60 μg. are summarised in the Table. The accuracy of individual results generally lies within ±0·3% of the absolute values. No extra precautions were necessary for the determination of ethoxyl groups. The time required to complete all the operations involved in a single determination, including weighing, is approx. 2—2½ hr.

Compound	Alkoxyl (%) * CH_3O	Alkoxyl (%) * C_2H_5O	No. of detmtns.	Max. error (absolute)	Min. error (absolute)	Δ †
α-Methyl-D-glucoside	16·00 (15·98)	—	9	−0·34	+0·04	0·20
Vanillin	20·49 (20·40)	—	11	+0·38	+0·03	0·16
Narcotine	22·58 (22·52)	—	9	−0·42	+0·03	0·23
Phenacetin	—	25·25 (25·15)	5	+0·30	−0·06	0·18
α-Methyl 2 : 3-*O*-dimethylglucoside	41·80 (41·89)	—	4	−0·37	+0·01	—
α-Methyl 2 : 3 : 4 : 6-*O*-tetramethylglucoside	52·47 (52·52)	—	2	−0·11	+0·01	—
3 : 4-Dimethylmannose monohydrate	27·53 (27·43)	—	3	+0·34	−0·04	—
p-Diethoxybenzene	—	54·31 (54·21)	3	+0·25	+0·04	—
p-Ethoxybenzoic acid	—	27·17 (27·11)	3	+0·19	+0·15	—
Methyl *p*-aminobenzoate	20·52 (20·51)	—	3	+0·17	−0·04	—

* Calculated value in parentheses. † Standard deviation.

Experimental

Reagents.—(1) Hydriodic acid (*d* 1·7), " AnalaR " grade, purified according to Steyermark.[4] (2) Phenol, " AnalaR " grade. (3) Sodium antimonyl tartrate, 10% aqueous solution; freshly prepared every 1 or 2 days. (4) Sodium acetate, 10% solution in glacial acetic acid. (5) Sodium acetate, 25% aqueous solution. (6) Bromine, iodine free. (7) Formic acid (90%), " AnalaR " grade. (8) Sulphuric acid, 1N-solution. (9) Sodium thiosulphate, 0·01N-solution. (10) Potassium iodide, 10% solution freshly prepared daily. (11) " Thyodene " indicator.

Apparatus.—The following apparatus was used in addition to that given in the Figure: (1) An electrically heated aluminium block. (2) An " Agla " brand all-glass micrometer syringe burette. (3) A magnetic stirrer. (4) A " daylight " electric lamp to provide uniform illumination for titrations.

Procedure.—The absorber was charged with 1 ml. of sodium acetate–acetic acid solution and 4 drops of bromine were added from a capillary dropper. The scrubber was filled with 8 ml. of sodium antimonyl tartrate solution and its side arm was stoppered. The sample was weighed by difference into a platinum cup and transferred to the reaction flask by dropping the cup through the B7 side arm. A clean platinum tetrahedron, 0·25 g. of phenol, and 0·5 ml. of hydriodic acid were then added, and the B7 cone was placed in position, after the joint had been moistened with the acid. The joint between the scrubber and the absorber was lubricated with Silicone grease and all ground-glass joints were secured by metal springs. Water was circulated through the condenser and the nitrogen supply was connected to the apparatus through the B7 side arm attached to the digestion flask. The needle valve connecting the cylinder to the apparatus was adjusted so that nitrogen flowed through the apparatus at a rate corresponding to 1 bubble per second in the scrubber.

The contents of the flask were gradually raised to boiling during 30 min. and then digested at 220° for 60 min. (<40% alkoxyl) or 90 min. (>40% alkoxyl) as required.

The apparatus was disconnected and the contents of the absorber were quantitatively transferred to a titration beaker by using a transference pipette and four 1 ml. portions of water for washing. A magnetic stirring bar was used to mix the solution whilst 0·5 ml. of 25% sodium acetate solution was added and a sufficient number of drops (*ca.* 5) of formic acid to destroy the bromine. The contents of the beaker were stirred for 10 min. to ensure quantitative reduction of the free bromine, after which 5 drops of 1N-sulphuric acid and 3 drops of potassium iodide solution were added. The iodine thus liberated was titrated with 0·01N-sodium thiosulphate; a microspatula-full of the Thyodene indicator was added immediately before the

[4] Steyermark, " Quantitative Organic Microanalysis," Blakeston Company, New York, p. 231 (1951).

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end-point.* A blank determination was carried out by a similar procedure without addition of sample. The original titre was corrected accordingly.

Factor: 1 μl. of 0·01N-$Na_2S_2O_3$ ≡ 0·05172 μg. of OMe ≡ 0·0751 μg. of OEt.

We are grateful to the D.S.I.R. and the Commonwealth Relations Office for the provision of research grants and to Mr. H. Cale for the construction of many pieces of glassware.

CHEMISTRY DEPARTMENT,
THE UNIVERSITY, BIRMINGHAM, 15. [*Received, April 17th*, 1957.]

* It is important that the solution should remain cold during titration and it is therefore advisable to chill it. It is also important to carry out the titration slowly and smoothly.

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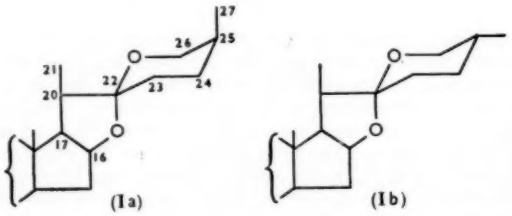
903. *The Stereochemistry of the Side-chain of the Steroidal Sapogenins: Configuration at $C_{(22)}$ of Normal and* iso-*Sapogenins.*

By R. K. CALLOW and (Miss) P. N. MASSY-BERESFORD.

3β-Acetoxy-5α-25*L*- and -25*D*-spirostan-23-one * have been prepared, and both have been converted, *via* the 24-bromo-derivatives, into 3β : 24-diacetoxy-5α-spirost-24-en-23-one. This provides chemical evidence that the normal and *iso*-sapogenins differ only in configuration at $C_{(25)}$. The absolute configuration of these compounds at $C_{(22)}$ is discussed.

THE natural steroid sapogenins occur in two isomeric series, the "normal" and "*iso*"-sapogenins, which differ in steric orientation in the side-chain, the former being converted into the latter by hydrogen chloride under certain conditions. Marker and Rohrmann [1] suggested that this isomerisation consists of a change of configuration at $C_{(22)}$ involving the opening and reclosure of ring F. Scheer, Kostic, and Mosettig [2] showed that the two series differ in configuration at $C_{(25)}$, and James [3] related the configuration at this asymmetric centre to glyceraldehyde, so that the "normal" and "*iso*"-series may be referred to as 25*L* (Ia) and 25*D* (Ib) respectively.



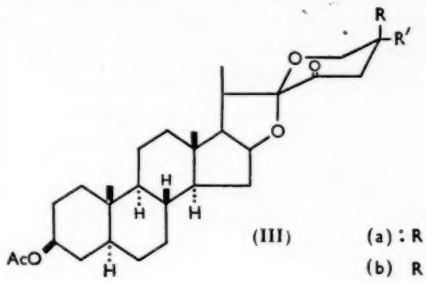
There remained the possibility that the two series differ in configuration at $C_{(22)}$ as well as at $C_{(25)}$. Scheer, Kostic, and Mosettig [4] later showed that dihydrosarsapogenin (IIa) and dihydrosmilagenin (IIb) differ only at $C_{(25)}$, but the possibility that inversion at $C_{(22)}$ had occurred during the opening of ring F could not be excluded. It has also been shown [5] that inversion at $C_{(25)}$ occurs without the opening of ring F, but as this is an unusual reaction further chemical evidence that the two series have the same configuration at $C_{(22)}$ was

* In this extension of the general convention, the capital italic *D* in 25*D* denotes that $C_{(27)}$ lies to the right when in a Fischer projection formula $C_{(24)}$ is written above, and $C_{(26)}$ is written below, $C_{(25)}$-25*L* denotes that in a similar projection formula $C_{(27)}$ lies to the left.—ED.

[1] Marker and Rohrmann, *J. Amer. Chem. Soc.*, 1939, **61**, 846.
[2] Scheer, Kostic, and Mosettig, *ibid.*, 1953, **75**, 4871.
[3] James, *J.*, 1955, 637.
[4] Scheer, Kostic, and Mosettig, *J. Amer. Chem. Soc.*, 1955, **77**, 641.
[5] Callow and James, *J.*, 1955, 1671.

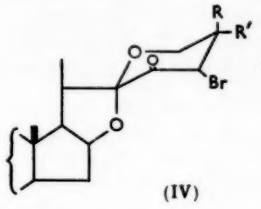
desirable. This could be obtained if two sapogenins, diastereoisomeric at position 25, could be converted, by reactions involving conditions under which isomerisation at $C_{(22)}$ is unlikely, into compounds in which the asymmetry at $C_{(25)}$ has been destroyed by introduction of a double bond between $C_{(25)}$ and an adjacent carbon atom. This has now been achieved: the identity of the unsaturated compounds obtained from *neo*tigogenin (25*L*) and tigogenin (25*D*) shows that there is only a single difference between these sapogenins, namely, the configuration at $C_{(25)}$.

Controlled oxidation of sarsasapogenin acetate by chromic acid yields a sapogenin, containing a ketone group in ring F, which Marker and Shabica [6] suggested was 23-oxo-sarsasapogenin acetate. This reaction seemed to offer a convenient entry into ring F, and its application to *neo*tigogenin and tigogenin acetates was investigated. These sapogenins yielded the previously undescribed 23-oxo-derivatives (IIIa and b), obtained pure by means of the special method of separation by use of reagent T, recommended by Girard and Sandulesco [7] for ketones of high molecular weight, in yields of 8·8% and 2·4%, respectively. The usual Girard procedure resulted in the formation of inseparable emulsions. The 23-oxo-compounds have an infrared band at 1727 cm.$^{-1}$, and show marked differences from the parent sapogenins in the "fingerprint" region. There is weak ultraviolet absorption at about 300 mμ (log ε 1·5). The ketones form crystalline semicarbazones. In the 25*D*-series the formation of the semicarbazone from the ketone is accompanied by a large increase in dextrorotation ($\Delta[M]_D$ +171°) whereas in the 25*L*-series there is a small change in the opposite direction ($\Delta[M]_D$ −44°). Huang-Minlon reduction of (IIIa and b) yields the parent sapogenins, showing that no configurational changes occurred during the oxidation by chromic acid.

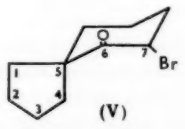


(III)

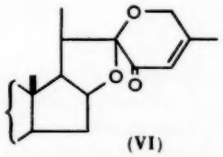
(a): R = Me, R′ = H (25*L*)
(b) R = H, R′ = Me (25*D*)



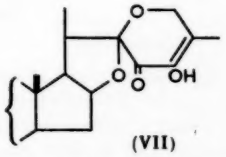
(IV)



(V)



(VI)



(VII)

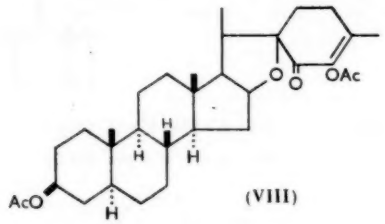
Crystalline 24-bromo-23-oxosapogenin acetates (IVa and b) were obtained in 30—40% yield by bromination in chloroform–acetic acid. Bromination caused a displacement of the infrared carbonyl absorption to a higher frequency (1745 cm.$^{-1}$) in both the 25*L*- and the 25*D*-compound, and the weak ultraviolet absorption is at 296 mμ (log ε 1·8). This is evidence [8,9] that the bromine has entered the equatorial position in both compounds. Although the preferred conformation for the C–Br bond in 2-bromo*cyclo*hexanones is axial,[10] steric repulsion between an axial bromine and other substituents suffices in some

[6] Marker and Shabica, *J. Amer. Chem. Soc.*, 1942, **64**, 813.
[7] Girard and Sandulesco, *Helv. Chim. Acta*, 1936, **19**, 1095.
[8] Jones, Ramsay, Herling, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 2828.
[9] Cookson, *J.*, 1954, 282.
[10] Corey, *J. Amer. Chem. Soc.*, 1953, **75**, 2301.

cases to overcome the electrostatic repulsion of the C–Br (equatorial) and C=O dipoles, with the result that the more stable conformation is that in which the bromine is equatorial. This is known to occur [10] in 7-bromo*spiro*[4 : 5]decan-6-one (V) which exists predominantly as the equatorial isomer. There would be considerable 1 : 3-interaction between an axial bromine atom and the 4-methylene group of the *cyclo*pentane ring. The 24-bromo-23-oxosapogenins (IVa and b) are structurally analogous, so there would be steric repulsion between an axial bromine atom at position 24 and the oxygen atom of ring E. The carbon–bromine absorptions appear at 670 and 697 cm.$^{-1}$, respectively, in CS_2 solution. The compounds (IVa and b) were debrominated by zinc dust in alcohol to give the parent ketones in good yield, so that no changes in the configuration of the side-chain had occurred during bromination.

Dehydrobromination of compounds (IVa and b) by boiling collidine gave very low yields of the αβ-unsaturated ketone (VI), especially from the latter, presumably owing to the *cis*-relation of the bromine and the hydrogen atom at $C_{(25)}$. This approach was abandoned when another route to 24 : 25-unsaturated derivatives proved successful.

Hydrolysis of compounds (IVa and b) by ethanolic potassium hydroxide at room temperature proceeded with simultaneous autoxidation of the α-ketols, to give, in both series, 3β : 24-dihydroxy-5α-spirost-24-en-23-one (VII), the enolic form of the 23 : 24-dioxosapogenins. This compound absorbs in the infrared at 1690(m) and 1660(s) cm.$^{-1}$ in $CHCl_3$ solution. It is suggested that the band at 1690 cm.$^{-1}$ is due to the αβ-unsaturated carbonyl group, and the band at 1660 cm.$^{-1}$ is the absorption of the same group when internally hydrogen-bonded. The hydroxyl absorption, consisting of two broad bands at about 3480 and 3100 cm.$^{-1}$ (KCl disc), also indicates strong hydrogen bonding in the solid state. The compound is surprisingly insoluble in methanol for a sapogenin derivative containing two hydroxyl groups. Its ultraviolet absorption is at 276 mμ (log ε 4·0). The autoxidation of the intermediate 24-hydroxy-23-oxosapogenins is analogous to that of benzoin to benzil [11] in alkaline solution in the presence of atmospheric oxygen.



(VIII)

The samples of the enol (VII) derived from *neo*tigogenin and tigogenin were converted into the 3β : 24-diacetate (VIII), and a detailed comparison of the two samples was made. They had identical melting points, optical rotations, infrared absorption spectra in $CHCl_3$ solution and in KCl discs, and ultraviolet absorption spectra, and single crystals of the two samples gave identical *X*-ray diffraction patterns. Thus *neo*tigogenin and tigogenin must differ only in configuration at $C_{(25)}$.

Some other reactions of the 23-oxosapogenins have been studied, but the low yields in which these compounds are obtainable prevented a thorough investigation of the less promising reactions.

Sodium borohydride in methanol reduces the 23-oxo-group, and crystalline 3β : 23-dihydroxy- and 3β-acetoxy-23-hydroxy-derivatives were obtained in both series. (No attempt was made to separate 23*a*- and 23*b*-isomers.) We had hoped that it would be possible to replace the 23-hydroxyl group by halogen, thus correlating the 23-oxosapogenins with the 23-halogenosapogenins obtained by direct halogenation. The results

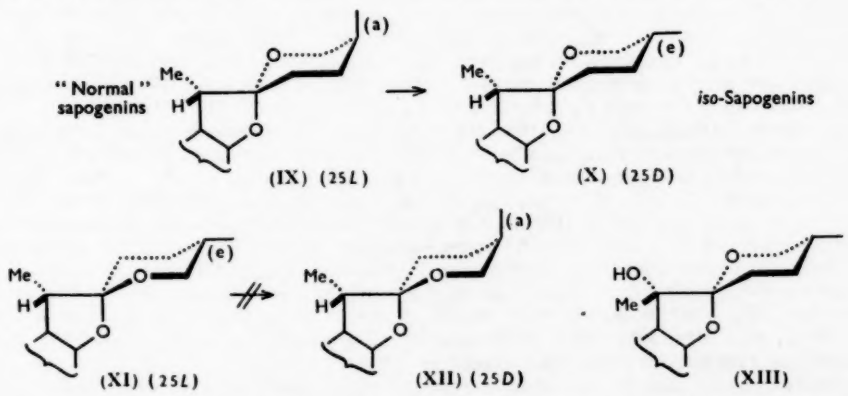
[11] Weissberger, *Ber.*, 1932, **65**, 1815.

were not encouraging. 3β-Acetoxy-23-hydroxy-5α-25*D*-spirostan with phosphorus pentachloride in carbon tetrachloride containing calcium carbonate in suspension yielded chlorine-containing gums whose infrared absorption did not resemble that of 23-chlorotigogenin acetate prepared by direct chlorination of tigogenin acetate. 3β-Acetoxy-23-hydroxy-5α-25*L*-spirostan was converted into the 23-methanesulphonate, and the gummy product treated with lithium bromide in various solvents: no replacement of the methanesulphonyloxy-group occurred, and there was evidence from infrared absorption that this treatment had destroyed the spiroketal system.

Attempts to prepare a *pseudo*-derivative of the ketone (IIIa) yielded gums which showed no infrared or ultraviolet absorption attributable to an αβ-unsaturated ketone.

Dr. Carl Djerrassi measured the optical rotatory dispersion curves of compounds (IIIa and b), (IVa and b), (VI), and (VIII) over the range 280—700 mμ, and has kindly given us permission to quote the results. The 23-oxosapogenins show similar curves with a positive peak at 330 mμ.[12] Since a change of configuration at $C_{(25)}$ would not be expected to cause an inversion of the curve, this is consistent with the configurational identity of the compounds at $C_{(22)}$. It was hoped that some information as to the absolute configuration about $C_{(22)}$ might be obtained from the curves for the 24-bromo-23-oxosapogenins, since for axial 24-bromo-23-ketones derived from (IX) and (X) the curves should be positive, while those derived from (XI) and (XII) should give negative rotatory dispersion curves irrespective of the orientation of $C_{(27)}$. The curves obtained confirmed the evidence from infrared and ultraviolet absorption spectra that the compounds are equatorial α-bromo-ketones, so that no conclusions could be drawn from the results.

The discussion of the configuration of the sapogenins at $C_{(22)}$ must take into account the relative stability of the two series as indicated by the conversion of normal into *iso*-sapogenins. It is logical to assume that this change at $C_{(25)}$ is a change from an axial conformation of the methyl group to an equatorial one. Application of the method of conformational analysis led us to conclusions mainly identical with those reached by Hirschmann *et al.*[13] In particular ring F is in a prone position with the 23 : 24-bond parallel to the 20 : 22-bond. The assignment of the α- or β-position to the $C_{(22)}$–O bond in ring F involves some uncertain assumptions of the strength of interactions, and Hirschmann *et al.* felt justified in assigning to this bond the β-position in the normal and the α-position



in the *iso*-sapogenins. Now, however, that it has been shown that the configuration at $C_{(22)}$ is the same in both series, it is clear that, with the absolute configuration at $C_{(25)}$

[12] See Djerassi and Klyne, *Proc. Chem. Soc.*, 1957, 55, for nomenclature.
[13] Hirschmann, Hirschmann, and Corcoran, *J. Org. Chem.*, 1955, **20**, 572.

known, the conformation of ring F with the methyl group axial is to be assigned to the normal sapogenins (IX), and the conformation with the methyl group equatorial to the *iso*-sapogenins (X), both these conformations having the oxygen atom in the α-position. If the oxygen atom were in the β-position, as in (XI) and (XII), the conformations of the methyl groups would be inconsistent with the known relative stability of the two series.

Wall and Walens * have shown that 20α-hydroxy-20-*iso*tigogenin (XIII) has the same configuration as tigogenin at $C_{(22)}$, and has an infrared absorption in the hydroxyl region indicative of strong hydrogen bonding, to be attributed to bonding between the oxygen atom of ring F and the 20α-hydroxyl group. This is additional evidence in favour of the α-position for the $C_{(22)}$–O bond in the natural sapogenins.

Experimental

M. p.s were determined in a Kofler apparatus with polarised light, and are corrected. Optical rotations were determined in $CHCl_3$ solutions of concentration 1·0% unless otherwise stated. Samples for analysis were recrystallised to constant m. p. and dried at 80°, 100°, or 140° in a high vacuum. Ultraviolet absorption spectra were measured in methanol. Infrared absorption was measured with a double-beam instrument with a rock-salt prism (Perkin-Elmer Model 21) in KCl discs unless otherwise stated.

23-Oxoneotigogenin Acetate.—*neo*Tigogenin acetate (10 g.) was oxidised with chromic acid in acetic acid solution at 60° by Fieser and Jacobsen's method.[14] Crystallisation of the neutral fraction from methanol separated the ketone and unchanged *neo*tigogenin acetate from lactone acetate which remained in the mother-liquors. The mixture of ketone and sapogenin acetates (1·6 g.) in ethanol (67·5 ml.) and glacial acetic acid (7·5 ml.), and Girard's reagent T (3·0 g.) were boiled under reflux for 2 hr. Ethylene glycol (67·5 ml.) was added and the ethanol evaporated under reduced pressure from the steam-bath. After cooling, the mixture was extracted six times with dry benzene, and the extracts were washed with glycol, then with water, dried, and evaporated, to give *neo*tigogenin acetate (0·68 g.). The glycol fractions were diluted with water, glacial acetic acid (50 ml.) was added, and the mixture heated at 100° for 3 hr. After cooling, the solid was collected, washed, and dried *in vacuo* over P_2O_5 (0·906 g., 8·8%). This method gives a complete separation of ketonic from non-ketonic material in one operation. Recrystallised from methanol, *23-oxoneotigogenin acetate* has m. p. 231—234°, $[\alpha]_D$ −49° (Found: C, 73·7; H, 9·4. $C_{29}H_{44}O_5$ requires C, 73·7; H, 9·4%), $\lambda_{max.}$ 302—304 mμ (log ε 1·5), $\nu_{max.}$ 1730 cm.$^{-1}$ (ketone and acetate). Hydrolysis of the acetate by 5% potassium hydroxide solution in boiling ethanol and recrystallisation from acetone–light petroleum (b. p. 60—80°) gave *23-oxoneotigogenin*, m. p. 244—247°, $[\alpha]_D$ −56° (*c* 0·78%) (Found: C, 75·2; H, 9·6. $C_{27}H_{42}O_4$ requires C, 75·3; H, 9·8%), $\lambda_{max.}$ 300—304 mμ (log ε 1·6), $\nu_{max.}$ 1727 cm.$^{-1}$, $\nu_{max.}$ (in CS_2) 1732 cm.$^{-1}$.

The acid fraction from the oxidation gave *neotigogenoic acid*, m. p. 212—216° (from methanol), $[\alpha]_D$ −153° (*c* 0·2%) (Found: C, 72·5; H, 9·5. $C_{27}H_{42}O_5$ requires C, 72·6; H, 9·5%), $\nu_{max.}$ 1737 ($C_{(16)}$-ketone), 1712 ($C_{(22)}$-ketone), 1680 cm.$^{-1}$ (internally hydrogen-bonded carboxyl group). Treatment with ethanolic 3% sodium hydroxide for 2 hr. under reflux gave *anhydroneotigogenoic acid*, m. p. 238—240° (from chloroform–ether), $[\alpha]_D$ −137° (*c* 0·56%) (Found: C, 75·4; H, 9·4. $C_{27}H_{40}O_4$ requires C, 75·7; H, 9·4%), $\lambda_{max.}$ 244 mμ (log ε 4·2), $\nu_{max.}$ 1715, 1693, 1660(s) cm.$^{-1}$.

23-Oxo*neo*tigogenin acetate (139 mg.) in ethanol (25 ml.) and a solution of semicarbazide hydrochloride (200 mg.) and sodium hydrogen carbonate (100 mg.) in water (1 ml.) were boiled for 7½ hr., then poured into water and extracted with chloroform, and the extract was washed, dried, and evaporated. Crystallised from ethyl acetate, the *semicarbazone* has m. p. 232—240° (decomp.), $[\alpha]_D$ −52° (Found: C, 67·7; H, 8·9; N, 7·8. $C_{30}H_{47}O_5N_3$ requires C, 68·0; H, 8·9; N, 7·9%), $\nu_{max.}$ 3430, 3260—3180, 1730 (acetate), 1700 (amide I, carboxyl), 1670 (C=N), 1580 (amide II), 1250 (acetate), 760 (NH rocking) cm.$^{-1}$.[15]

23-Oxotigogenin Acetate.—Tigogenin acetate (10 g.), prepared from hecogenin acetate and freed from traces of the latter by Girard separation, was oxidised as described for *neo*tigogenin

* We are indebted to Dr. Walens for the personal communication of their results before publication (*Chem. and Ind.*, 1957, 818).

[14] Fieser and Jacobsen, *J. Amer. Chem. Soc.*, 1938, **60**, 28.

[15] Davison and Christie, *J.*, 1955, 3389.

acetate but at 70—90°. Girard separation by the special method described above, yielded 1·83 g. of tigogenin acetate and 0·53 g. of crude 23-oxotigogenin acetate, purified from further traces of hecogenin acetate by crystallisation from methanol (yield of pure ketone 247 mg., 2·4%). *23-Oxotigogenin acetate* has m. p. 233—235° (from methanol), $[\alpha]_D$ −53° (Found: C, 73·7; H, 9·1%), $\lambda_{max.}$ 298—300 mμ (log ε 1·5), $\nu_{max.}$ 1730 cm.$^{-1}$. Hydrolysis of the acetate gave *23-oxotigogenin*, m. p. 232—234° (from methanol), $[\alpha]_D$ −43° (Found: C, 75·0; H, 9·7%), $\lambda_{max.}$ 300—302 mμ (log ε 1·5), $\nu_{max.}$ 1722 cm.$^{-1}$, $\nu_{max.}$ (in $CHCl_3$) 1730 cm.$^{-1}$. *23-Oxotigogenin acetate semicarbazone*, prepared as described for the 25*L*-derivative, has m. p. 212—215° (from ethyl acetate), $[\alpha]_D$ −15° (Found: C, 67·9; H, 9·0; N, 7·8%), $\nu_{max.}$ 3420, 3100, 2960, 1725, 1694, 1575, 1250, 755 cm.$^{-1}$.

Huang-Minlon Reduction of 23-Oxo*neo*tigogenin *Acetate*.—23-Oxo*neo*tigogenin acetate (200 mg.), ethylene glycol (50 ml.), potassium hydroxide (6·5 g.), water (6·5 ml.), and hydrazine hydrate (100%; 5 ml.) were boiled under reflux for 2 hr. The water and excess of hydrazine were then distilled off, and the mixture boiled at 195° for 2 hr. After cooling, it was poured into water, and neutralised, and the solid collected, washed, and dried *in vacuo* over P_2O_5. The product was chromatographed and yielded 168 mg. (95%) of *neo*tigogenin which, after recrystallisation, had the elementary composition, m. p., $[\alpha]_D$, and infrared absorption of authentic material.

Huang-Minlon Reduction of 23-Oxotigogenin.—This was carried out as described above. 206 mg. of 23-oxotigogenin yielded 190 mg. (95%) of crude tigogenin which, after recrystallisation, had the elementary composition and physical properties of authentic material.

Bromination of 23-Oxo*neotigogenin Acetate*.—To a solution of 23-oxo*neo*tigogenin acetate (894 mg., 1·89 mmoles) in chloroform (20 ml.) and glacial acetic acid (40 ml.) stirred at 35°, were added 3 drops of concentrated hydrobromic acid and then 3·42 mmoles of bromine (17·5 ml. of a 1% v/v solution of bromine in glacial acetic acid) during 20 min. The solution was stirred at room temperature for 1 hr., poured into water, and extracted with chloroform. The extract was washed with sodium hydrogen carbonate solution until free from acid, then with thiosulphate solution and with water, dried, and evaporated under reduced pressure at room temperature. The black gum was chromatographed on neutral alumina. Benzene–light petroleum (b. p. 60—80°) (2 : 3) eluted the α-bromo-ketone (471 mg., 45%). Crystallisation from methanol gave *24-bromo-23-oxoneotigogenin acetate*, m. p. 190—194° (decomp.), $[\alpha]_D$ −76° (Found: C, 63·1; H, 8·0; Br, 14·3. $C_{29}H_{43}O_5Br$ requires C, 63·2; H, 7·9; Br, 14·5%), $\lambda_{max.}$ 297 mμ (log ε 1·9), $\nu_{max.}$ 1745 (shoulder; C=O), 1728 (acetate), 1260 (acetate), 750, 660 (C−Br) cm.$^{-1}$, $\nu_{max.}$ (in CS_2) 749, 670, 606, 586, 530 cm.$^{-1}$.

Bromination of 23-Oxotigogenin Acetate.—23-Oxotigogenin acetate (820 mg.) was brominated at 42° and chromatographed as described above, and yielded 302 mg. (32%) of material which recrystallised from methanol to give *24-bromo-23-oxotigogenin acetate*, m. p. 211—216°, $[\alpha]_D$ −60° (Found: C, 63·4; H, 8·1; Br, 14·7%), $\lambda_{max.}$ 296 mμ (log ε 1·8), $\nu_{max.}$ 1743 (shoulder), 1732, 1250, 695 (C−Br), 657 cm.$^{-1}$, $\nu_{max.}$ (in CS_2) 743(w), 697, 662, 614 and 606 (doublet), 579(w), 532 cm.$^{-1}$.

Debrominations.—24-Bromo-23-oxo*neo*tigogenin acetate (75 mg.) in ethanol (50 ml.) was boiled under reflux with stirring for 3 hr. with zinc dust (3 g.). The zinc was filtered off and the filtrate evaporated to give 23-oxo*neo*tigogenin acetate (70 mg.) which, after two recrystallisations, gave analytical figures and had physical properties identical with those of an authentic sample.

Similar debromination of 24-bromo-23-oxotigogenin acetate gave 23-oxotigogenin acetate in high yield, identical with an authentic sample.

Hydrolyses.—A solution of 24-bromo-23-oxo*neo*tigogenin acetate (286 mg.) and potassium hydroxide (3 g.) in water (15 ml.) and ethanol (115 ml.) was stirred at room temperature for 3 hr. Carbon dioxide was then passed into the solution until the pH was about 8, water was added, and the solution extracted with chloroform. The extract was washed with 2N-sodium carbonate and water, dried, and evaporated and the residue (145 mg., 63%) crystallised from methanol to give plates of 3β : *24-dihydroxy-5α-spirost-24-en-23-one*, m. p. 263—273°, $[\alpha]_D$ −88° (*c* 0·44%) (Found: C, 72·6; H, 9·0. $C_{27}H_{40}O_5$ requires C, 72·9; H, 9·1%), $\lambda_{max.}$ 276 mμ (log ε 4·0), $\nu_{max.}$ 1685(m), 1657(s), $\lambda_{max.}$ (in $CHCl_3$) 1690(m), 1662(s) cm.$^{-1}$. The aqueous layer from the hydrolysis and the carbonate washings were acidified to give an unidentified acid fraction (51 mg.).

24-Bromo-23-oxotigogenin acetate (411 mg.) was hydrolysed as described above, and the product (0·26 g., 78%) recrystallised, to give the same enol, m. p. 263—273°, $[\alpha]_D$ −85° (*c* 0·42%)

(Found: C, 72·9; H, 9·5%), $\lambda_{max.}$ 275 mμ (log ε 4·0), $\nu_{max.}$ 1685, 1658, $\nu_{max.}$ (in $CHCl_3$) 1695(m), 1664(s) cm.$^{-1}$. The aqueous layers yielded 130 mg. of unidentified acidic material.

3β : 24-*Diacetoxy*-5α-*spirost*-24-*en*-23-*one*.—Samples of 3β : 24-dihydroxy-5α-spirost-24-en-23-one derived from *neo*tigogenin and tigogenin were acetylated in pyridine–acetic anhydride (1 : 1) at room temperature. The solvents were evaporated under reduced pressure from the steam-bath, and the residues dissolved in carbon tetrachloride, evaporated to dryness six times, and recrystallised from methanol after treatment with a little neutral charcoal. The products had the following properties: (*a*) 3β : 24-*Diacetoxy*-5α-*spirost*-24-*en*-23-*one* (from *neo*tigogenin), m. p. 220—226°, $[\alpha]_D$ −95° (Found: C, 70·3; H, 8·7. $C_{31}H_{44}O_7$ requires C, 70·4; H, 8·4%), $\lambda_{max.}$ 242 mμ (log ε 4·0), $\nu_{max.}$ 1770 (vinyl acetate), 1728 (acetate), 1702 and 1668 (αβ-unsaturated ketone), 1250 (acetate), 1198 (vinyl acetate), 765 cm.$^{-1}$; (*b*) (from tigogenin), m. p. 222—226°, $[\alpha]_D$ −95° (Found: C, 70·4; H, 8·4%), $\lambda_{max.}$ 242 mμ (log ε 4·0), $\nu_{max.}$ 1765, 1725, 1700, 1665, 1250, 1197, 762 cm.$^{-1}$.

Reduction of the 23-*Oxosapogenin Acetates by Sodium Borohydride*.—To the 23-oxosapogenin acetate (100 mg.) in methanol (50 ml.) was added a solution of sodium borohydride (20 mg.) in water (1 ml.) and methanol (4 ml.) and, after the evolution of hydrogen had ceased, the mixture was boiled for 15 min., and poured into water. The solid was collected, washed, dried *in vacuo* over P_2O_5, and recrystallised from acetone–light petroleum (b. p. 80—100°).

3β-*Acetoxy*-23-*hydroxy*-5α-25L-*spirostan* has m. p. 188—204°, $[\alpha]_D$ −80° (Found: C, 73·5; H, 9·8. $C_{29}H_{46}O_5$ requires C, 73·4; H, 9·8%), $\nu_{max.}$ 3450, 1725, 1250 cm.$^{-1}$, hydrolysed by ethanolic 5% potassium hydroxide to 3β : 23-*dihydroxy*-5α-25L-*spirostan*, m. p. 218—230° [from acetone–light petroleum (b. p. 60—80°)], $[\alpha]_D$ −77° (Found: C, 74·6; H, 10·1. $C_{27}H_{44}O_4$ requires C, 74·9; H, 10·3%), $\nu_{max.}$ 3440 cm.$^{-1}$.

3β-*Acetoxy*-23-*hydroxy*-5α-25D-*spirostan* has m. p. 203—213°, $[\alpha]_D$ −59° (Found: C, 73·0; H, 9·9%), $\nu_{max.}$ 3400, 1735, 1250 cm.$^{-1}$, and is hydrolysed to 3β : 23-*dihydroxy*-5α-25D-*spirostan*, m. p. 222—226° [from acetone–light petroleum (b. p. 80—100°)], $[\alpha]_D$ −65° (Found: C, 74·7; H, 9·9%), $\nu_{max.}$ 3300 cm.$^{-1}$.

Dehydrobrominations.—24-Bromo-23-oxo*neo*tigogenin acetate (240 mg.) was boiled under reflux with collidine (20 ml.) for 2 hr. The collidine was then evaporated under reduced pressure and the residue taken up in chloroform, washed with dilute hydrochloric acid, sodium hydrogen carbonate solution, and water, and dried. Evaporation gave a brown residue which was percolated through neutral alumina in benzene–light petroleum (b. p. 60—80°) (1 : 2), yielding a mixture (199 mg.) of α-bromo-ketone and αβ-unsaturated ketone. This was chromatographed on alumina (Spence Type H); benzene–light petroleum (b. p. 60—80°; 1 : 2) eluted the α-bromo-ketone, and benzene–light petroleum (1 : 1) eluted αβ-unsaturated ketone (58 mg.). Two recrystallisations from methanol gave plates of 3β-*acetoxy*-5α-*spirost*-24-*en*-23-*one*, m. p. 237—246°, $[\alpha]_D$ −84° (Found: C, 73·5; H, 9·1. $C_{29}H_{42}O_5$ requires C, 74·0; H, 9·0%), $\lambda_{max.}$ 233 mμ (log ε 4·1), $\nu_{max.}$ 1732 (acetate), 1682 and 1643 (αβ-unsaturated ketone), 1250 (acetate), 894, 871, 847 cm.$^{-1}$ (trisubstituted double bond).

24-Bromo-23-oxotigogenin acetate (204 mg.) was dehydrobrominated as described above. Chromatography on alumina (Spence Type H) did not completely separate unchanged starting material. The fractions (22 mg.) containing the αβ-unsaturated ketone were recrystallised three times from methanol, to give material (5 mg.) of m. p. 234—236°, $\lambda_{max.}$ 232 mμ (log ε 3·9), $\nu_{max.}$ 1730, 1690, 1645, 1250, 893, 873, 850 cm.$^{-1}$. *X*-Ray diffraction patterns of single crystals of this material, and of 3β-acetoxy-5α-spirost-24-en-23-one described above were similar, but not identical. Further purification was not attempted.

We are indebted to Dr. J. W. Cornforth for many helpful discussions, Dr. C. Djerassi for the optical rotatory dispersion curves, Dr. J. E. Page for infrared absorption spectra of the 24-bromo-23-oxosapogenins in the low-frequency range, Mrs. O. Kennard for the *X*-ray diffraction photographs, and Miss Patricia Dodson for technical assistance.

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[*Received, June 7th,* 1957.]

XUM

904. *The 720 cm.$^{-1}$ Band in the Infrared Spectra of Crystalline Long-chain Compounds.*

By D. Chapman.

A correlation between the appearance of the band associated with the CH_2 rocking mode in the 720 cm.$^{-1}$ region of the spectra of crystalline long-chain compounds and the type of packing of the chains is discussed.

Recently it has been suggested [1] that a doublet observed in the 720 cm.$^{-1}$ region of the infrared spectrum of some long-chain compounds can be correlated with orthorhombic packing of the hydrocarbon chains, whilst a single band in this region can be correlated with hexagonal or triclinic packed chains. As this correlation may be more usefully and generally extended, it is now considered in greater detail.

Although theory and discussion [2-8] have mainly concerned the appearance of a doublet in the 720 cm.$^{-1}$ region of the infrared spectra of Polythene and *n*-paraffins many other long-chain crystals exhibit it. Indeed this doublet has been observed so frequently that Bellamy [9] states that the band (associated with a CH_2 rocking vibration) can be distinguished from other bands in this region by observing whether it is single in the spectrum of the liquid and double in the crystalline state. However, several long-chain compounds do show only a single band in this region, *e.g.*, the β_L-form of triglycerides.[10]

In long-chain crystals the unit cells may contain one, two, or more layers. Chains without any one layer are almost always parallel to one another. They may be either normal or inclined to the basal plane. The arrangement of chains in layers depends essentially on their end groups. If we disregard the end groups a layer of chains can be regarded as composed of repeating units (sub-cells [11]). For simple structures one sub-cell suffices to describe the arrangement within a layer: for more complicated structures more than one type of sub-cell may be present.

The structures of long-chain crystals so far investigated have been described in terms of two main types of sub-cell.[12,13] The more important is the orthorhombic sub-cell (Fig. 1) which is common to the structures of $C_{29}H_{60}$ hydrocarbon and Polythene (von Sydow [13]). The packing-environment of a hydrocarbon chain in the orthorhombic sub-cell of a long-chain crystal such as the *B* and *C* forms of stearic acid is therefore identical with that which occurs in the orthorhombic paraffin. Since the 720 cm.$^{-1}$ doublet in the spectra of the orthorhombic paraffin is attributed to interaction between neighbouring chains, we may expect that similar interaction will occur with other long-chain compounds containing an orthorhombic sub-cell. The doublet is observed in the infrared spectra of many long-chain compounds (Table 1) which have this type of sub-cell.

The correlation is striking, yet it is possible that a long-chain molecule may pack in an orthorhombic manner without causing the appearance of a doublet, *e.g.*, when the dimensions of the sub-cell are larger than normal, or when distortions occur in the cell, since then the interaction between chains may be too small to give a resolvable splitting. (The extent of splitting depends on the nature and magnitude of the forces involved.) However,

[1] Chapman, Sixth International Spectroscopic Colloquium, Amsterdam, 1956.
[2] Thompson and Torkington, *Proc. Roy. Soc.*, 1945, *A*, **184**, 3.
[3] Elliot, Ambrose, and Temple, *J. Chem. Phys.*, 1948, **16**, 877.
[4] Stein and Sutherland, *ibid.*, 1954, **23**, 1993.
[5] Stein, *ibid.*, 1955, **23**, 734.
[6] Keller and Sandemann, *J. Polymer Sci.*, 1955, **15**, 133.
[7] Krimm, Liang, and Sutherland, *J. Chem. Phys.*, 1956, **25**, 543.
[8] Tobin, *J. Chem. Phys.*, 1955, **23**, 891.
[9] Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, London, 1954.
[10] Chapman, *J.*, 1956, 2522.
[11] Vand, *Acta Cryst.*, 1951, **4**, 104.
[12] Daniel, *Adv. Phys.*, 1953, **2**, 450.
[13] von Sydow, *Arkiv Kemi*, 1956, **9**, 231.

where two components equal or nearly equal in intensity are observed, it is plausible to predict that the hydrocarbon chains have orthorhombic packing. This packing has been recently predicted for the hydrocarbon chains of the β_L'-form of triglycerides,[14] whose spectra show a doublet at 727 and 719 cm.$^{-1}$.

TABLE 1. *Compounds showing the doublet near 727 and 719 cm.$^{-1}$ in the spectrum of their stable crystalline form and their hydrocarbon-chain packing.*

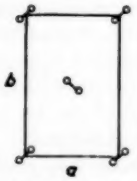
Monocarboxylic Acids.—C_{16} (*B* form), O*; C_{18} (*C* form) O*; C_{20}, CH; C_{16}, CH; C_{14}, CH; C_{18} (*B'* form), O*; C_{17} (*B'* form), CH; C_{19} (*B'* form), CH; C_{21} (*B'* form), CH.
Others.—Octadecyl alcohol, O†; octadecyl palmitate, O†; hexadecanedicarboxylic acid, O†; long-chain methyl esters (*e.g.*, methyl stearate), probably O‡; long-chain ethyl esters (*e.g.*, ethyl stearate), probably O‡.

O, Orthorhombic; CH, crystallographically homologous.
The main *X*-ray short spacings ‡ of long-chain methyl and ethyl esters are at *ca.* 3·7 and 4·2 Å whilst those of hydrocarbons in the orthorhombic form are at *ca.* 3·8 and 4·2 Å.
* von Sydow, ref. 13. † Schoon, *Z. phys. Chem.*, 1938, *B*, **39**, 385. ‡ Malkin, "Progress in the Chemistry of Fats and other Lipids," Pergamon Press, London, 1952, Vol. 1, p. 14.

An important variant on the orthorhombic sub-cell is obtained when the angle θ between the diagonals is 60°, *i.e.*, the basal figure is a regular hexagon (Fig. 2). This hexagonal form, corresponding to the best packing of cylindrical rods, was discovered by Muller [15] who noted that there was only a single strong short-spacing at 4·12 Å in the *X*-ray powder photograph of certain long-chain hydrocarbons. He postulated that, in this form of sub-cell, rotation of the hydrocarbon chain occurs about its long axis; this has been confirmed.[18] Other long-chain compoinds also exhibit this hexagonal form, *e.g.*, long-chain ethyl esters,[17], 1-monoglycerides [17] and triglycerides.[17] The spectra [1,4] of the hexagonal form of all these molecules show a strong single band at 720 cm.$^{-1}$.

The reason for the appearance of only a single band at 720 cm.$^{-1}$ can be understood if we note that the chains in this sub-cell are in a more symmetrical environment than in the orthorhombic sub-cell. The chains in the hexagonal sub-cell will tend to equivalence so that there will be effectively only one chain per primitive sub-cell and hence only one

FIG. 1.



Orthorhombic

FIG. 2.

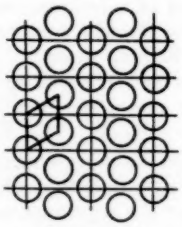
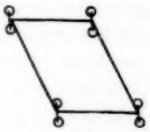

Hexagonal

FIG. 3.


Triclinic

component of each fundamental vibration will be allowed (cf. Tobin [8]). Furthermore, apart from symmetry considerations, the interchain distance in the hexagonal form is practically the same as in the liquid (where, it is suggested, the chains pack in a square array). For hexatriacontane the distances are 4·86 Å in the liquid and 4·85 Å in the hexagonal form, to be compared with the smaller interchain distance [18] in the orthorhombic sub-cell of 4·47 Å. Although the chains in the hexagonal form may rotate in an analogous fashion to a closed set of gear wheels,[16] the average interaction due to the large interchain

[14] Chapman, *J.*, 1957, 2715.
[15] Muller, *Proc. Roy. Soc.*, 1932, *A*, **138**, 5.
[18] Andrew, *J. Chem. Phys.*, 1950, **18**, 607.
[17] Malkin (*a*) *Trans. Faraday Soc.*, 1933, **29**, 977; (*b*) "Progress in the Chemistry of Fats and other Lipids," Pergamon Press, London, 1954, Vol. 2.
[18] Vand, *Acta Cryst.*, 1953, **6**, 797.

distance must be considerably less than in the orthorhombic sub-cell, so that even if two components were allowed their separation would be negligible (cf. Stein [5]). (The large sub-cell also probably explains why the band is at 720 cm.$^{-1}$ in the unperturbed position.)

The second main type of sub-cell is the triclinic cell (Fig. 3) which occurs in the β_L-form of trilaurin.[19] In this sub-cell all the planes of zig-zag are parallel to one another, whilst making an angle ϕ with the *a*-axis. In this sub-cell the environment of any hydrocarbon chain is different from that occurring in the orthorhombic sub-cell so that we might expect that a doublet at 720 cm.$^{-1}$ will not be observed with this type of packing. Further, whilst there are two chains in the orthorhombic sub-cell, and hence two components of each fundamental vibration are possible, in the triclinic sub-cell there is only one chain and hence only one component of each fundamental vibration is possible (cf. Tobin [8]).

Some compounds which have triclinic packed hydrocarbon chains are given in Table 2. The shift in the band from the unperturbed position at 720 cm.$^{-1}$ to 717 cm.$^{-1}$ probably arises because of a change in the internal potential energy function of the molecule due to the equilibrium field of the crystal, which in turn is due to the van der Waals forces

TABLE 2. *Compounds showing a strong single band in the* 720 *cm.*$^{-1}$ *region of the spectrum of their stable crystalline form, and their hydrocarbon-chain packing.*

Octadecane, T *	T	CH
silver stearate, T †	T	CH
trilaurin (β_L form), T ‡	T	CH
tristearin (β_L form), CH	T	CH
tripalmitin (β_L form), CH	T	CH
1-palmitodistearin (β_L form), CH	T	CH
1-stearodipalmitin (β_L form), CH	T	CH
stearo-oleostearin (β_L form), CH	T	CH
myristic acid (*A* form), T §	T	CH
pentadecanoic acid (*A'* form), T §	T	CH

T, triclinic; CH, crystallographically homologous.

* Muller and Lonsdale, *Acta Cryst.*, 1948, **1**, 129. † Vand, Aitken, and Campbell, *ibid.*, 1949, **2**, 398. ‡ Ref. 19. § Ref. 13.

operative in the sub-cell. A decrease in the frequency of a band is quite commonly observed when a change from the liquid to the crystal phase occurs.

The orthorhombic and triclinic sub-cells are by far the most important known. Indeed, von Sydow states that these are the only two types present in covalent normal-chain compounds.[14]

In general, we can conclude that for these two types of sub-cell, particularly for the orthorhombic type, there appears to be a good correlation between the appearance and position of the band in the 720 cm.$^{-1}$ region and the type of sub-cell. This may prove useful in predicting the type of hydrocarbon-chain packing in long-chain crystals before their more definitive *X*-ray analysis of single crystals.

Finally, there is a third and unusual (and so far unique) type of sub-cell discovered by Vand, Lomer, and Lang [20] in the crystal structure of the *A*-form of potassium hexanoate. This differs from other sub-cells in that the chain axes (as distinct from zig-zag planes) are not all parallel. They cross one another within the same layer so that the zig-zags of neighbouring chains fit one another. The spectrum of potassium hexanoate in this form shows only a single band at 717 cm.$^{-1}$, with a weaker additional band at 737 cm.$^{-1}$.

We thank Dr. N. Sheppard for an interesting discussion, and the directors of Unilever Limited for permission to publish this work.

UNILEVER LIMITED, PORT SUNLIGHT, CHESHIRE. [*Received, April 29th,* 1957.]

[19] Vand and Bell, *Acta Cryst.*, 1951, **4**, 465.
[20] Vand, Lomer, and Lang, *ibid.*, 1949, **2**, 214.

905. *The Alkaline Degradation of Polysaccharides. Part I. Soluble Products of the Action of Sodium Hydroxide on Cellulose.*

By G. N. Richards and H. H. Sephton.

The major soluble products of the degradation of cotton hydrocellulose by boiling, oxygen-free 0·5N-sodium hydroxide have been identified and in several cases their relative amounts have been determined. D-Gluco*iso*-saccharinic and formic acid are produced in greatest amount under the conditions used.

Much of the earlier structural work on polysaccharides, particularly the starches and hemicelluloses, was carried out on materials which had been subject to vigorous alkaline treatments. Recent work on the alkaline degradation of *O*-substituted hexose derivatives [1] indicated, however, that this type of treatment, particularly of a polysaccharide containing 1 : 3-, 1 : 4-, or 1 : 6-glycosidic links, is likely to result in stepwise degradation from the reducing end of the molecule. Nevertheless the generalisations derived from the work on *O*-substituted hexoses suggest possible application in the determination of polysaccharide structure by alkaline degradation. For example the nature of the saccharinic acid product is dependent on the position of substitution, *i.e.*, the position of the polysaccharide linkage, and the effect of branch points on alkaline degradation should be specific and to some extent predictable. These generalisations, however, were mostly derived from experiments in lime-water at room temperature, which were made in order to simplify the reaction systems involved, and little is yet known of the effects of other alkalis and the higher temperatures which have often been used in alkaline treatments of polysaccharides.

For work on polysaccharides, cotton cellulose was the obvious choice since its structure and reactivity have been much studied. Further, it combines chemical and stereochemical purity with ready availability. Alkaline degradation of cellulose in the hot alkaline refining of wood pulps for the rayon industry causes considerable losses of α-cellulose, but no extensive systematic study has yet been made of the soluble products of this reaction system, and much of the work on wood pulps has been complicated by degradation of hemicelluloses.

Davidson's original suggestion [2] that attack by alkali occurs only at the reducing end of the cellulose molecule has received much further experimental support. Thus it has been shown that modification of the reducing end-group by oxidation,[3a] reduction,[3b] or glycosidation [3c] can render cellulose stable to alkali, and it is known [4] that D-gluco*iso*-saccharinic acid is a major product. Theories of saccharinic acid formation [5] are in accord with this, and more particularly it has been shown [6] that cellotetraose in lime-water undergoes the expected stepwise degradation from the reducing end, which leads to *iso*saccharinic acid. However, D-gluco*meta*saccharinic,[4c] formic, acetic, lactic, and glycollic [7] acid are also produced by alkaline degradation of cellulosic materials, and it seemed probable that other types of alkaline degradation occurred simultaneously, affording a complex mixture of products.

The aim of the present work was to identify and determine the relative amounts of the most important products of the degradation of cellulose by hot, dilute, aqueous sodium

[1] Kenner and Richards, *J.*, 1957, 3019, and earlier references.
[2] Davidson, *J. Textile Inst.*, 1934, **25**, T174.
[3] Meller, *TAPPI*, (*a*) 1952, **35**, 72; (*b*) 1953, **36**, 366; (*c*) Reeves, Schwartz, and Giddens, *J. Amer. Chem. Soc.*, 1946, **68**, 1383.
[4] (*a*) Murumow, Sack, and Tollens, *Ber.*, 1901, **34**, 1427; (*b*) Richtzenhain and Abrahamsson, *Svensk Papperstidn.*, 1954, **57**, 538; (*c*) Green, *TAPPI*, 1956, **39**, 472.
[5] (*a*) Isbell, *J. Res. Nat. Bur. Stand.*, 1944, **32**, 45; (*b*) Kenner, *Chem. and Ind.*, 1955, 727, and references therein.
[6] Corbett and Kenner, *J.*, 1955, 1431.
[7] Chesley, Montgomery, and Sandborn, U.S.P. 2,750,414.

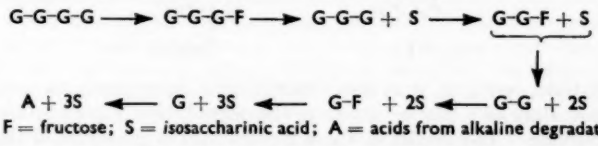
hydroxide (conditions corresponding approximately to those of rayon pulp-refining). Cotton hydrocellulose was chosen as substrate because its method of preparation and high crystallinity gave maximum probability of normal end-groups to each molecule, and chemical uniformity along the chains. In order to reduce possible secondary rearrangements of primary products of the degradation, reactions were restricted to relatively short times, and oxygen was excluded in order to avoid possible autoxidation of reactive intermediates. Thus hydrocellulose was boiled with oxygen-free 0·5N-sodium hydroxide for 30 min., and the soluble products were isolated and identified as indicated in the Experimental section, the results being summarised in Table 1. The rapid formation of γ-lactones in presence of a sulphonic acid-substituted resin, and subsequent partial separation of lactonisable from non-lactonisable acids, is noteworthy.

TABLE 1. *Soluble acids from treatment of hydrocellulose with 0·5N-sodium hydroxide at 100°.*

Acid	R_L value (solvent *a*)	Identification [a]	Yield (% carbon return)
Unidentified acid [*]	0·34	P.C.	
Unidentified lactone	0·43	P.C.	
β-D-Gluco*meta*saccharinic	0·52 (lactone)	P.C.	
αβ-D-Gluco*iso*saccharinic	0·58 (lactone) 0·19 (acid)	C.	*ca.* 44
βγ-Dihydroxybutyric [*]	0·60	P.C.	
C_5 *meta*-Saccharinic	0·69 (lactone)	P.C.	
αβ-Dihydroxy-α-methylpropionic	0·70	P.C.	
Glycollic	0·74	C.	
Unidentified acid	0·80	P.C.	
α-D-Glucosaccharinic ‡	0·82 (lactone)	P.C.	
Lactic	1·00	C.	4·3
Dihydroxybutyric	1·02 (lactone)	P.C.	
Lactyl-lactic	1·11	P.C.	
Formic	(Volatile)	C.	7—8
Acetic	(Volatile)	T.	<2

[*] Reacts rapidly with spray *b*. † May conceal traces of α-D-gluco*meta*saccharinic acid.
‡ May also include C_5 *meta*saccharinolactone.
[a] P.C. = paper chromatography; C = crystalline derivative; T = qualitative test.

Many of the minor products, particularly lactic acid, are known to be produced in considerable amount by the alkaline degradation of glucose under these conditions, and in this respect it is particularly important to realise the effect of complete degradation of a given cellulose molecule. It follows from Corbett and Kenner's results [6] that this would liberate the non-reducing end-unit of the molecule as glucose:



(G = glucose; F = fructose; S = *iso*saccharinic acid; A = acids from alkaline degradation of glucose.)

This will be more important if the soluble oligosaccharides either extracted or produced during the degradation are degraded more rapidly than the insoluble cellulose. The glucose liberated would undergo degradation and rearrangement which, under the prevailing conditions, would be expected [8] to yield mainly lactic acid. To investigate the importance of this effect the hydrocellulose was separated into fractions of high and low degree of polymerisation (D.P.) by the method commonly used for α-cellulose determination, and the relevant fractions are therefore referred to as α- and β-hydrocellulose respectively. Both fractions contained only the cellulose II crystalline structure and it is assumed that any contribution from degradation of the non-reducing end-group would be emphasised in the composition of the products of degradation of the β-fraction. The

[8] (*a*) Shaffer and Friedemann, *J. Biol. Chem.*, 1930, **86**, 345; (*b*) Evans, *Chem. Rev.*, 1942, **31**, 537.

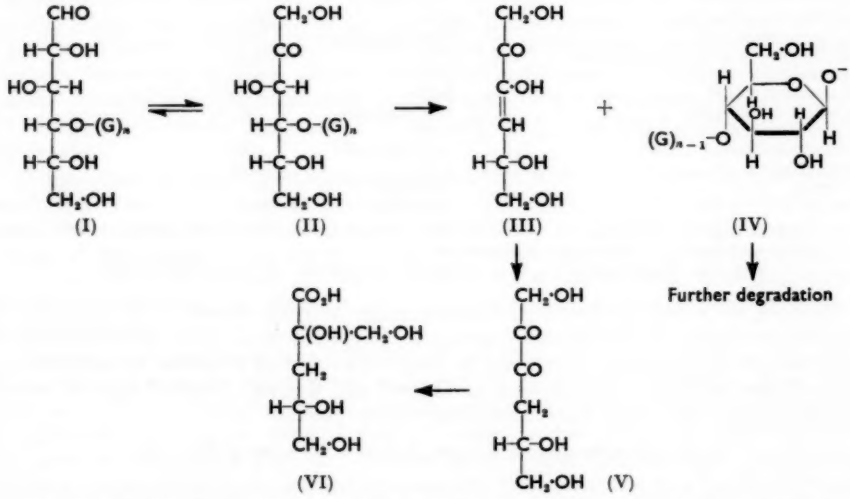
production of formic and lactic acid on alkaline degradation of these fractions is recorded in Table 2.

TABLE 2. *Degradation of α- and β-hydrocellulose by* 0·5N-*sodium hydroxide.*

	α-Hydrocellulose			β-Hydrocellulose		
Time (min.)	Total acid (meq./g.)	Formic acid (%)	Lactic acid (%)	Total acid (meq./g.)	Formic acid (%)	Lactic acid (%)
5	0·15	27	6·0	0·8	27	5·7
10	—	—	—	1·1	—	5·3
15	0·3	28	6·2	1·4	—	5·7
30	0·5	29	6·0	2·0	35	5·4
240	0·9	34	6·8	—	—	—

Discussion.—The present results leave no doubt that D-gluco*iso*saccharinic acid (VI) is the major product of the degradation of cellulose by hot dilute sodium hydroxide.

Infrared analysis of the non-volatile acids, and periodate oxidation of the lactonisable acids, confirmed this, and quantitative paper chromatography indicated a carbon return of approximately 44% as this acid under the prevailing conditions. The sequence of reactions leading to formation of this acid and resulting in progressive stepwise degradation of the cellulose molecule (I) from the reducing end-group has been discussed by Corbett and Kenner.[6]

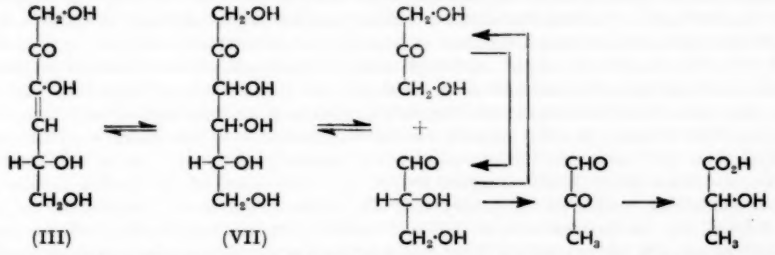


For the first time, however, it is now evident that other products are formed to the extent of approximately 56% carbon return in the degradation of pure cellulose by oxygen-free sodium hydroxide. The results in Table 2 show that degradation of the non-reducing end-group does not contribute to the formation of this mixture of acids, and the observed lactic acid could not arise by a reversed aldol condensation of the fructosyl intermediate (II) (cf. ref. 9) since ionisation of the 4-hydroxyl group is prevented by substitution. In the case of the keto-enol (III), however, it is reasonable to suppose that a slow, competing addition of hydroxyl anion might occur, leading to formation of a ketohexose mixture (VII), alkaline degradation of which would yield a mixture containing mostly lactic acid, together with most of the acids in Table 1.

The observed relative yields of lactic acid are much lower than those recorded by Chesley *et al.*[7] for similar degradations at 240°, although the yields of acetic and formic acid were similar in both systems. This indicates that several types of reaction, having very

[9] Kenner and Richards, *J.*, 1954, 1784, and references therein.

different activation energies, may be involved. It is probable that there are additional sources of most of the other products, the most likely being degradation and rearrangement of the diketone (V), fragmentation of the reducing end-group (I), or an alternative degradation of the substituted glucosyl anion (IV).



Formic acid is evidently a particularly important product and its yield both in relation to those of total acids and of acetic acid is quite different from that obtained by similar alkaline degradation of glucose.[8b] Certain possibilities regarding its formation can, however, be eliminated. There is no indication of the formation of appreciable amounts of free formaldehyde during the reaction—it was not detected, for example, in the volatile neutral products. Also the complete absence of methanol from the products eliminates the possibility that formic acid arose by a Cannizzaro reaction between two molecules of formaldehyde; and similarly a crossed Cannizzaro reaction between formaldehyde and another monocarbonyl compound would be expected to yield a stable product in sufficient amount to permit its detection. The possibility that small amounts of unremoved atmospheric oxygen were causing oxidation of the reducing end-grouping to formic acid and a substituted arabonic acid is eliminated by the results of the succeeding paper.

Experimental

The following solvents and sprays were used for paper chromatography on Whatman No. 1 paper at 25°: solvents *a*,[10] ethyl acetate–acetic acid–water (10 : 1·3 : 1); *b*, ethanol–aq. ammonia (*d* 0·88)–water (8·5 : 1·4 : 1); *c*,[11] butan-1-ol–ethanol–water (4 : 1·1 : 1·9). Sprays *a*,[12] hydroxylamine–ferric chloride; *b*,[13] sodium metaperiodate–potassium permanganate; *c*,[14] B.D.H. "4·5" indicator; *d*,[15] bromophenol-blue–citric acid; *e*,[16] 1% solution of diphenylamine in acetic acid–concentrated sulphuric acid (39 : 1 freshly prepared); *f*,[17] silver nitrate–sodium hydroxide.

Analytical Methods.—(a) *Formic acid.* 0·1N-Formic acid (50 ml.) was distilled to dryness under reduced pressure from a bath at 60°, a splash-head being used to avoid spray contamination, and the distillate collected in a receiver at 0°. Water (5 ml.) was added to the residue and the whole again evaporated to dryness, and this was repeated twice more. Titration of the distillate and residue indicated that all but 2·5% of the formic acid distilled under these conditions. Similar treatment of a lactic acid solution yielded 10% of the acid in the distillate.

Volatile acids from hydrocellulose degradations were boiled under reflux for 2½—3 hr. with an excess of red mercuric oxide. Experiments with authentic samples indicated that this procedure completely removed formic acid, while having no effect on acetic acid, which could be titrated in the resulting solution after filtration. The similar procedure described by Evans and Hass,[18] in which the solution was boiled for only 30 min., resulted in complete destruction of formic acid only when freshly prepared yellow mercuric oxide was used.

(b) *Lactic acid.* Hullin and Noble's procedure [19] was applied with the omission of the lime

[10] Richtzenhain and Moilanen, *Acta Chem. Scand.*, 1954, **8**, 704.
[11] Hough, Jones, and Wadman, *J.*, 1950, 1702.
[12] Abdel-Akher and Smith, *J. Amer. Chem. Soc.*, 1951, **73**, 5859.
[13] Lemieux and Bauer, *Analyt. Chem.*, 1954, **26**, 920.
[14] Nair and Muthe, *Naturwiss.*, 1956, **43**, 106.
[15] Kennedy and Barker, *Analyt. Chem.*, 1951, **23**, 1033.
[16] Cf. Dische, *Microchemie*, 1930, **8**, 4.
[17] Trevelyan, Procter, and Harrison, *Nature*, 1950, **166**, 444.
[18] Evans and Hass, *J. Amer. Chem. Soc.*, 1926, **48**, 2708.
[19] Hullin and Noble, *Biochem. J.*, 1953, **55**, 289.

treatment. Addition of known amounts of lactic acid to the products of alkaline degradation of hydrocellulose and subsequent determination by this method gave the expected increases, so it was assumed that other products did not interfere. The procedure gave no colour with relevant amounts of authentic α-D-gluco*iso*saccharinic and glycollic acid, and with formic acid gave only a small optical density at 5650 Å.

(c) *Glycollic acid.* Calkins's procedure,[20] when applied to the products of alkaline degradation of hydrocellulose, yielded a solution with maximum absorption at 4650 Å, compared with 5300 Å for authentic glycollic acid. Although this procedure with relevant amounts of authentic α-D-gluco*iso*saccharinic, formic, and lactic acid did not lead to colour formation, addition of known amounts of glycollic acid to the degradation products and subsequent treatment by this method indicated that it was not suitable for the determination of glycollic acid in this case.

Preparation of Cotton Limit Hydrocellulose.—Chemically untreated Sudan-sakel cotton in the form of carded sliver (kindly supplied by Dr. G. F. Davidson of the Shirley Institute) was cut into short lengths, boiled vigorously with 1% sodium hydroxide solution (40 ml./g.) for 8 hr., filtered, and washed with water. The scoured cotton was then boiled with stirring with 2N-hydrochloric acid (40 ml./g.) for 3 hr., the solution decanted from the cellulose powder, an equal volume of fresh acid added, and boiling continued for a further 3 hr. The final product was filtered off, washed with water until neutral and then with ethanol and ether, and dried (P_2O_5) as a fine, white powder.

Fractionation of Hydrocellulose.—Cotton hydrocellulose (80 g.) was stirred gently under nitrogen at room temperature for 1 hr. with 17·5% sodium hydroxide solution (500 ml.) and then diluted by the slow addition of water (375 ml.). After being kept at 0° overnight the solid α-hydrocellulose was separated by centrifuging, washed with water, dilute hydrochloric acid, and water again, and finally with acetone and ether and dried at 0·1 mm. (P_2O_5) as a white powder (25 g.; D.P. 291 by viscosity of cuprammonium solution; *X*-ray diffraction indicated only cellulose II lattice present).

A further sample (80 g.) of hydrocellulose was treated with 17·5% aqueous sodium hydroxide for 1 hr. as above, diluted by the slow addition of water (4·5 l.), and kept at 0° overnight. The liquor was separated by centrifuging and adjusted to pH 5 by the slow addition of concentrated hydrochloric acid with vigorous stirring. The resultant gelatinous precipitate was separated next morning, dialysed, washed with acetone and ether, and dried as above (yield 20 g.). β-Hydrocellulose was a light, pale yellow powder of D.P. 135 (cuprammonium), and *X*-ray diffraction indicated only the cellulose II lattice.

Alkaline Degradation of Hydrocellulose: *Qualitative Analysis.*—(a) *Volatile products.* An aqueous suspension of hydrocellulose (48·2 g. in 700 ml.) was boiled in a stream of nitrogen with stirring under reflux for 15 min. Oxygen-free 7·5N-sodium hydroxide (50 ml.) was then added and boiling and stirring continued for a further 30 min. in an atmosphere of nitrogen. The resulting suspension was cooled under nitrogen, then filtered, and the solid washed with water (500 ml.), followed by ethanol and ether, and dried (P_2O_5) (yield 43·1 g.). The filtrate and aqueous washings were combined, stirred with freshly washed Amberlite resin IR-120(H) (200 ml.) for 10 min., then passed through a column of the same resin (200 ml.). The acidic effluent and subsequent washings were combined (1990 ml.), an aliquot portion was treated with an equal volume of 0·1N-sodium hydroxide (4-fold excess) at room temperature for 30 min., and then titrated with 0·1N-hydrochloric acid to phenolphthalein. The total acid yield thus determined was 42·8 meq.

The remaining acidic solution (1970 ml.) was boiled and stirred under reflux with excess of calcium carbonate for 10 min., then cooled, filtered, and evaporated to dryness under reduced pressure (yield 6·14 g.); some insoluble black resin (*ca.* 0·1 g.) which separated during the evaporation was rejected. The first portion (50 ml.) of the distillate was collected at −20° and gave a negative test for methanol.[21] To the remainder of the distillate was added concentrated hydrochloric acid (350 ml.), followed by a saturated solution of 2 : 4-dinitrophenylhydrazine in 2N-hydrochloric acid (350 ml.). After 24 hr. at room temperature the resultant orange-coloured precipitate (0·32 g.) was separated (filtrate A) and recrystallised from anisole and then nitrobenzene as fine brown needles, m. p. 245—246° (decomp.) (Found: C, 45·0; H, 3·2; N, 21·5%). After a further 10 days at room temperature the filtrate (A) had deposited a further precipitate (0·24 g.) (m. p. 280°) which, when recrystallised from nitrobenzene as an orange powder, had

[20] Calkins, *Analyt. Chem.*, 1943, **15**, 762.
[21] Denigès, *Compt. rend.*, 1910, **150**, 832.

m. p. 301° (decomp.) alone or in admixture with the pyruvaldehyde derivative (Found: C, 42·1; H, 2·9; N, 25·5. Calc. for $C_{15}H_{12}O_8N_8$: C, 41·7; H, 2·8; N, 25·9%).

The syrupy calcium salts were next dissolved in water and passed through a column of Amberlite resin IR-120(H) (50 ml.). The total acidity of the resulting solution, determined by back-titration of excess of alkali as above, corresponded to 40·0 meq. after completion of sampling. This solution was evaporated to dryness as described above for the determination of formic acid; the total acidity of the distillate by direct titration with sodium hydroxide then corresponded to 14·5 meq., of which 12·5 meq. was formic acid.

Determination of formic acid in an aliquot portion of a solution of the residue from distillation, by boiling with mercuric oxide as above, indicated the presence of a further 0·6 meq. A portion of the distillate was next boiled under reflux for 3 hr. with excess of mercuric oxide, filtered, neutralised with calcium carbonate and evaporated to dryness. The residue gave qualitative tests for acetic and lactic acid. A further portion of the distillate was neutralised with sodium hydroxide, concentrated, and converted into 4-bromophenacyl formate in the usual way. Recrystallised from aqueous ethanol this had m. p. and mixed m. p. 133—134°.

(b) *Preliminary examination of non-volatile acids and identification of* α-D-*glucoisosaccharinic acid.* Part of the residue (1·0 g.) from the foregoing distillation was boiled with water (10 ml.) containing excess of calcium hydroxide for 5 min., cooled, and filtered. The filtrate was saturated with carbon dioxide, boiled for 5 min., again cooled, and filtered. The resulting solution was decolorised with charcoal, concentrated to *ca.* 5 ml., and kept at 0° overnight. A small amount (0·06 g.) of calcium α-D-glucoisosaccharinate separated and was converted by treatment with Amberlite resin IR-120(H) into the crystalline lactone, m. p. and mixed m. p. 91·5—92·5° after one recrystallisation from ethyl acetate–light petroleum.

Calcium salts were precipitated from the mother-liquors of the above crystallisation by gradual addition of ethanol but, apart from a concentration of the D-glucoisosaccharinates in the earlier fractions, no effective fractionation was observed The fractions were treated with Amberlite resin IR-120(H) and examined by paper chromatography in solvent *a* with sprays *a*, *b*, and *c*. The acids which were tentatively identified by this method and by similar chromatography in subsequent experiments are indicated in Table 1 with their R_L values (L = lactic acid): D-glucoisosaccharinic acids were clearly the major products, while the minor products were all apparently present in comparable amount. Authentic reference compounds were normally chromatographed in presence of an excess of D-glucoisosaccharinolactone, since this often affected the R_L values.

(c) *Identification of lactic acid.* A sample of the total non-volatile acids (7·20 g.), obtained as described above, was shaken at room temperature for 10 min. each with three portions (each 20 ml.) of dry ether. The combined extracts were evaporated to dryness, to yield a viscous liquid (0·20 g.) which by paper chromatography in solvent *a* (sprays *a*, *b*, *c*) contained components corresponding to lactic and lactyl-lactic acid, a dihydroxybutyrolactone, and αβ-D-glucoisosaccharinolactone. This syrup was then extracted by shaking for 10 min. at room temperature with three portions (2·5 ml. each) of 9 : 1 ether–*n*-hexane. The extract contained almost pure lactic and lactyl-lactic acid (0·05 g.) which readily gave 4-bromophenacyl lactate, m. p. and mixed m. p. 112—113°.

(d) *Identification of glycollic acid.* Part of the residue (4·30 g.) from the ether-extraction in (c) was further dried at 50°/0·01 mm. over phosphoric oxide for 1 hr. and then dissolved in water (250 ml.). Direct titration to pH 7 showed the presence of 8·4 meq. of free acid, while back-titration of excess of alkali as in (a) indicated 25·7 meq. of total acid. The remaining solution (245 ml.) was stirred at room temperature for 15 min. with Amberlite resin IRA-400 (carbonate form; 25 ml.) and then passed through the same sample of resin in a column during 15 min. The column was subsequently washed with water (25 ml.), the total effluent combined, excess of aqueous ammonia added, and the whole evaporated to dryness. The residue (B) was shown by paper chromatography in solvent *b* (sprays *b*, *d*) to contain mainly D-glucoisosaccharinic acids (R_L *ca.* 0·58). Glycollic (R_L *ca.* 0·72) and lactic acid (R_L 1·00) were also detected and possibly resisted removal by the resin owing to cross- or self-esterification.

The resin carbonate was eluted with N-ammonium carbonate (200 ml.) during 2 hr. and the eluate and washings were evaporated to dryness. A solution of the residue in water (20 ml.) was stirred for 15 min. with Amberlite resin IR-120(H) (20 ml.), then filtered, and the resin washed with water. The filtrate and washings were concentrated to 10 ml., and back-titration after treatment of an aliquot portion with excess of alkali indicated the presence of 0·85 meq. of

acid per ml. Part of this solution (7·5 ml.) was transferred uniformly to two sheets of Whatman No. 3 mm. paper (56 × 61 cm.) and eluted with solvent *a* for 7 hr. at 25°. Indicator strips (causing 6% loss) were treated on alternate sides with sprays *a* and *c*, and the band corresponding to glycollic acid eluted with water. A band intermediate between the glycollic acid and the *iso*saccharinolactone zone contained mixed acids and was rejected. The eluate contained 0·70 meq. of acid (by direct titration with sodium hydroxide), and readily yielded 4-bromophenacyl glycollate, m. p. and mixed m. p. 138—140° after recrystallisation from benzene. Paper chromatography of the eluate indicated mainly glycollic acid with only traces of the supposed α-D-glucosaccharinolactone.

Elution of the relevant band yielded 0·38 meq. of chromatographically pure lactic acid, but lactyl-lactic acid was lost by elution from the bottom of the paper during chromatography. Elution of a band from the origin to a position of R_L 0·4 yielded 0·76 meq. of acid by back-titration of excess of alkali, and this material, when examined as ammonium salts by paper chromatography in solvent *b*, was found to contain D-gluco*iso*saccharinolactone (R_L *ca.* 0·58), and glycollic (R_L *ca.* 0·76), and lactic acids (R_L 1·00), presumably arising by alkaline hydrolysis of " cross-esters."

(e) *Identification of* D-*gluco*iso*saccharinic acids.* A solution (250 ml.) of the ammonium salt residue (B) from the previous experiment was stirred with Amberlite resin IR-120(H) (40 ml.) at room temperature, while at intervals aliquot portions were titrated with 0·01N-sodium hydroxide (phenolphthalein, transient end-point). Total acids were determined by back-titration and lactonisation calculated as follows: 20% (0·5 hr.); 31% (1·5 hr.); 39% (3·0 hr.); 44% (4·5 hr.); 56% (21 hr.); 56·5% (26·5 hr.). After 27 hr. the solution was filtered and stirred for 1 hr. with Amberlite resin IRA-400 (carbonate) (40 ml.) (pH 4·3), then filtered again and shown by back-titration of excess of alkali to contain 7·1 meq. (0·0220 meq./ml.) of lactonised acid (losses by sampling) (solution L).

Part of the solution (300 ml.) was stirred with excess of calcium hydroxide at 60° for 30 min., then filtered, saturated with carbon dioxide, and concentrated to 50 ml. After a further filtration and subsequent concentration to 5 ml. the solution was kept at 0° overnight; calcium α-D-gluco*iso*saccharinate (0·30 g.) then crystallised and was converted in almost theoretical yield into the crystalline lactone, m. p. and mixed m. p. 90—92° (from ethyl acetate–light petroleum). The mother-liquors containing calcium salts were evaporated to dryness (0·90 g.) and crystallisation of the residue from a small amount of water yielded a further amount of the above α-isomer (0·24 g.). The remaining mother-liquors were treated with Amberlite resin IR-120(H) and then brucine in the usual manner, to yield the brucine salts, which crystallised readily from 95% ethanol. The product (0·32 g.) when recrystallised from the same solvent showed m. p. 152—153° alone or in admixture with authentic brucine α-D-gluco*iso*saccharinate (Found: C, 60·2; H, 6·8; N, 4·9. Calc. for $C_{29}H_{38}O_{10}N_2$: C, 60·6; H, 6·7; N, 4·9%).

Fractional precipitation by ether of the mother-liquors from crystallisation of the brucine salts yielded small amounts of later fractions which, when recrystallised several times from ethanol and ether, had m. p. 185—195°, not depressed by admixture with authentic brucine β-D-gluco*iso*saccharinate (Found: N, 5·2%).

(f) *Periodate oxidation of the lactonisable acids.* Part of the lactone solution (L) (25 ml.) from the previous experiment was treated with N-sodium hydroxide (1 ml.) at 60° for 5 min., cooled, and neutralised to pH 9 with hydrochloric acid. 0·2M-Sodium metaperiodate (20 ml.) was next added, and the solution diluted to 50 ml. and kept at room temperature. At intervals aliquot portions (5 ml.) were added to 10% sulphuric acid (10 ml.) containing potasium iodide (1 g.) and titrated with 0·1N-sodium thiosulphate. Periodate was consumed as follows: 2·9 (0·5 hr.); 4·1 (3·0 hr.); 4·4 (6·0 hr.); 4·8 (24 hr.) moles/equiv.

Similar treatment of authentic α-D-gluco*iso*saccharinolactone gave the following results: 2·8 (0·5 hr.); 3·8 (1·5 hr.); 4·3 (3·0 hr.); 4·7 (6·0 hr.); 4·9 (24 hr.) moles/equiv.

(g) *Non-volatile neutral products.* Hydrocellulose (50 g.) was treated with boiling 0·5N-sodium hydroxide (150 ml.) for 15 min. as in (a) above (acid yield 57·2 meq.; recovery of cellulose 43·6 g.). The acidic solution (1 l.) resulting from subsequent treatment with Amberlite resin IR-120(H) was stirred with Amberlite resin IRA-400 (carbonate form, 150 ml.) for 2 hr., then filtered, and the filtrate was stirred overnight with De-acidite FF (carbonate form, micro-bead, 2% cross-linked) (25 ml.). The conductivity of the solution was then 10^{-6} mho and after filtration evaporation gave a colourless syrup (0·16 g.).

Paper chromatography in solvent *c* indicated the following components: (i) corresponding

to glucose (R_F 0·075) (eliminated by treatment of the mixture with glucose dehydrogenase); (ii) corresponding to fructose (R_F 0·08); (iii) reacting as 2-deoxy-D-ribose (R_F 0·34) with spray *e* (blue coloration on heating); (iv) reacting with spray *f* (R_F 0·39), main component; (v), (vi), (vii), reacting with spray *f* (R_F 0·45, 0·54, 0·59); (viii), (ix), reacting on paper with silver nitrate in acetone (R_F 0·70, 0·80).

Elution of a small amount of fractions (viii) and (ix) with water from a paper chromatogram and examination of ultraviolet absorption of the resulting solutions gave absorption maxima as follows: (viii) 2600 Å, shifting to 2950 Å in alkali; (ix) 2450—2500 Å, shifting to 3100 Å in alkali.

Alkaline Degradation of Hydrocellulose: Quantitative Analysis.—(a) *Formic and lactic acid from α- and β-hydrocellulose.* In a typical experiment the hydrocellulose sample (0·5—1·5 g. of α-fraction; 0·25 g. of β-fraction) was heated with oxygen-free 0·5N-sodium hydroxide (10 ml. per g. of α-fraction; 20 ml. per g. of β-fraction) in a stoppered glass tube immersed in a boiling-water bath for the appropriate time. The mixture was then cooled, freshly washed Amberlite resin IR-120(H) (1 ml. per ml. of alkali) added, the whole shaken for 15 min., then filtered, and the resin washed until the filtrate totalled 100 ml. The total acidity of the solution was determined by back-titration of excess of alkali as above, and after suitable dilution of an aliquot portion lactic acid was determined as above. A further aliquot portion of the solution (75 ml.) was distilled and formic acid determined as described above. The results are expressed in Table 2. Probably owing to the heating conditions and absence of agitation the reproducibility of the total acid yield, relative to the amount of hydrocellulose, was *ca.* ±4%. The formic acid yields do not include undistilled formic acid (see above).

(b) D-*Glucoisosaccharinic acid.* A sample of the non-volatile acids obtained by alkali degradation of hydrocellulose as described above was dissolved in water, and the solution shown, by back-titration of excess of alkali, to contain 1·16 meq. of acid per ml. An aliquot portion (1·5 ml.) of this solution was transferred uniformly to a sheet of Whatman No. 3 mm. paper (56 × 61 cm.) and eluted with solvent *a* for 12 hr. at 20°. Suitable indicator strips were treated with sprays *a* and *c* on alternate sides of the paper, and the bands corresponding to α,β-D-gluco*iso*saccharinic acid and its lactone were eluted with water (25 ml., 50 ml. respectively). The acid in each solution was determined by back-titration of excess of alkali and corresponded to 0·09 (acid band) and 0·58 (lactone band) meq. The solution obtained by elution of the lactone band gave a positive test for glycollic acid and contained 0·10 meq. of free acid, determined by direct titration with alkali. Since an aqueous solution of authentic α-D-gluco-*iso*saccharinolactone contained no appreciable amount of free acid after storage at room temperature for 1 day, it is assumed that this free acidity is due to other acids. Besides the lactone, traces of free acids were detected by rechromatographing the concentrated eluates in solvents *a* and *b*.

The above chromatographic separation was repeated with a solution prepared by treatment of calcium α-D-gluco*iso*saccharinate with Amberlite resin IR-120(H) in water. 1·215 Meq. of the acid were added to the paper, of which 0·07 meq. was recovered in the acidic band and 0·77 meq. (0·02 meq. as free acid) in the lactone band, corresponding to a total recovery of 69%. Application of the appropriate factors to the recovery of D-gluco*iso*saccharinic acid from the previous experiment indicates that the maximum yield of this acid corresponds to 55% of the total non-volatile acid equivalents, or 48% after allowance for free acids as above. These figures were in reasonable agreement with a semi-quantitative infrared absorption analysis of a sample of the non-volatile acids, comparison being with an amorphous sample of α,β-D-gluco-*iso*saccharinolactone which had been purified by chromatography on carbon–Celite. The analysis was carried out on an absorption band thought to be connected with the lactone ring system, and the proportion of lactone in the mixture was determined by direct and back-titration in the usual manner.

The authors are grateful to M. J. Blears for extensive assistance in the experimental work, to Dr. H. J. Marrinan for the infrared analysis, to Dr. A. Sharples for D.P. determinations, and to Mr. H. J. Wellard for *X*-ray analysis. This work forms part of the programme of fundamental research undertaken by the council of the British Rayon Research Association. One author (H. H. S.) is a guest worker from the South African Council for Scientific and Industrial Research.

THE BRITISH RAYON RESEARCH ASSOCIATION, HEALD GREEN LABORATORIES,
WYTHENSHAWE, MANCHESTER, 22. [*Received, June 11th*, 1957.]

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906. *The Alkaline Degradation of Polysaccharides. Part II.* The Alkali-stable Residue from the Action of Sodium Hydroxide on Cellulose.*

By G. Machell and G. N. Richards.

The alkali-stable polysaccharide resulting from the treatment of cotton hydrocellulose with hot dilute, oxygen-free sodium hydroxide has been partially hydrolysed and D-gluco*meta*saccharinic acids isolated and identified. α-D-Glucosaccharinic acid was tentatively identified by paper chromatography. It is concluded that these acids originate by alkaline rearrangement of the reducing end-group of the cellulose molecule and so impart stability to alkali.

Degradation of cellulose by boiling dilute sodium hydroxide ultimately yields a polysaccharide which is stable to oxygen-free alkali,[1] and in view of the extensive losses of α-cellulose which occur, for example, in the hot alkali refining of wood-pulps [2] there is technological interest in the nature of the alkali-stable material. Richtzenhain *et al.*[1] have shown that the extent of degradation taking place before the attainment of alkali-stability is related to the degree of polymerisation of the original cellulose, and consequently to the number of reducing end-groups at which the degradation is known to commence. Further, there is evidence [3] that alkali stability is induced by conversion, during the degradation, of a normal reducing glucose end-group into a carboxylic acid, and two suggestions have been made as to the nature of this acid, although no attempt has been made to identify it. Richtzenhain and Abrahamsson [4] pointed out that a reducing end-group might undergo rearrangement to a saccharinic acid, while still remaining attached to the cellulose molecule, whereas Lindberg [5] was of the opinion that the alkali-stability may be due to oxidation of the reducing end-groups to carboxyl groups, either by traces of oxygen or by a "crossed" Cannizzaro reaction between the end-group and a soluble carbonyl degradation product. The latter type of reaction might also produce sorbitol as the end-unit of the chain, and this would also result in alkali-stability. However, Richtzenhain *et al.*[1] have also suggested that the ultimate alkali-stability may have a physical rather than a chemical cause.

The aim of the present work was to isolate and identify the alkali-stable end-group or groups. Alkali-stable hydrocellulose was prepared by degrading cotton hydrocellulose in 0·5N-sodium hydroxide at 100° in the absence of oxygen, conditions comparable to those of Richtzenhain *et al.*,[1] and the degradation was accompanied by a slight increase in the weight-average degree of polymerisation (D.P.). This increase, although occurring in a reaction which involves progressive shortening of cellulose molecules and a weight loss of more than 50%, is not unexpected. The system may be related to the acidic hydrolysis of hydrocellulose; here the D.P. falls only very slightly over a considerable range of weight loss, and Sharples [6] has shown that the effective hydrolysis occurs only at the ends of the cellulose micelles, causing a progressive shortening analogous to that postulated for the alkaline degradation. The resultant lack of effect on the weight-average D.P. depends on the molecular-weight distribution in hydrocellulose.[6] The observed increase in D.P. during alkaline degradation may therefore result from a combination of this effect with a preferential alkaline extraction of material of low D.P.

* Part I, preceding paper.

[1] Cf., *e.g.*, Richtzenhain, Lindgren, Abrahamsson, and Holmberg, *Svensk Papperstidn.*, 1954, **57**, 363.
[2] Cf., *e.g.*, Richter, *TAPPI*, 1955, **38**, 129.
[3] Samuelson and Wennerblom, *Svensk Papperstidn.*, 1954, **57**, 827; Clibbens, Geake, and Ridge, *J. Textile Inst.*, 1927, **18**, T277.
[4] Richtzenhain and Abrahamsson, *Svensk Papperstidn.*, 1954, **57**, 538.
[5] Lindberg, *ibid.*, 1956, **59**, 531.
[6] Sharples, *Trans. Faraday Soc.*, 1957, **53**, 1003.

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The presence of carboxylic acid groups in the product was demonstrated by its ability to absorb methylene-blue, but the relation of this absorption to an absolute carboxyl content is in doubt, particularly in the present instance where the acidic groups must be concentrated at the extremities of the cellulose micelles and so possibly not wholly accessible to a stoicheiometric interaction with the methylene-blue.

The initial step in the isolation of the group responsible for alkali-stability was acidic hydrolysis of the alkali-stable hydrocellulose, and Sharples's observations [6] on the acidic hydrolysis of hydrocellulose suggested that hydrolysis by a dilute, non-swelling mineral acid would preferentially dissolve end-units from the micelles. Further, Rogovin *et al.*[7] have shown that cellobiose and cellobionic acid are hydrolysed at similar rates, from which it follows that the presence of an aldonic acid type of grouping would not materially affect the rate of hydrolysis of the neighbouring glycosidic link. Probably therefore comparatively mild hydrolysis of the alkali-stable hydrocellulose would remove sufficient of the acidic end-grouping to permit its isolation. Accordingly, alkali-stable hydrocellulose was hydrolysed in N-hydrochloric acid at 100° for varying times, and the fall in methylene-blue absorption determined. The results are shown in Table 1. It was observed that the

TABLE 1. *Acidic hydrolysis of alkali-stable hydrocellulose.*

Hydrolysis (hr.)	Methylene-blue absorption (mmoles/100 g.) Initial	After NaOH treatment	Hydrolysis (hr.)	Methylene-blue absorption (mmoles/100 g.) Initial	After NaOH treatment
0	3·9	—	4	1·8	2·3
1	2·4	3·4	7	1·7	2·2
2	2·0	2·9	17	1·3	1·3

methylene-blue absorption of the hydrolysed alkali-stable hydrocellulose increased on treatment with 0·1N-sodium hydroxide in the cold, which does not affect hydrocellulose itself. This is unlikely to be due to hydrolysis of lactones since the latter would probably be decomposed in the methylene-blue solution, which is buffered at pH 8.[8] It is possible, however, that this effect may indicate esterification of the acidic end-group by glucose in the hydrolysis medium, followed by release of the polysaccharide acid on treatment with alkali.

In accordance with the observation of Richtzenhain *et al.*,[1] when alkali-stable hydrocellulose, from which most of the alkali-stable groups had been removed by a more stringent hydrolysis, was again treated with alkali at 100°, it suffered the same extent of degradation as the original hydrocellulose.

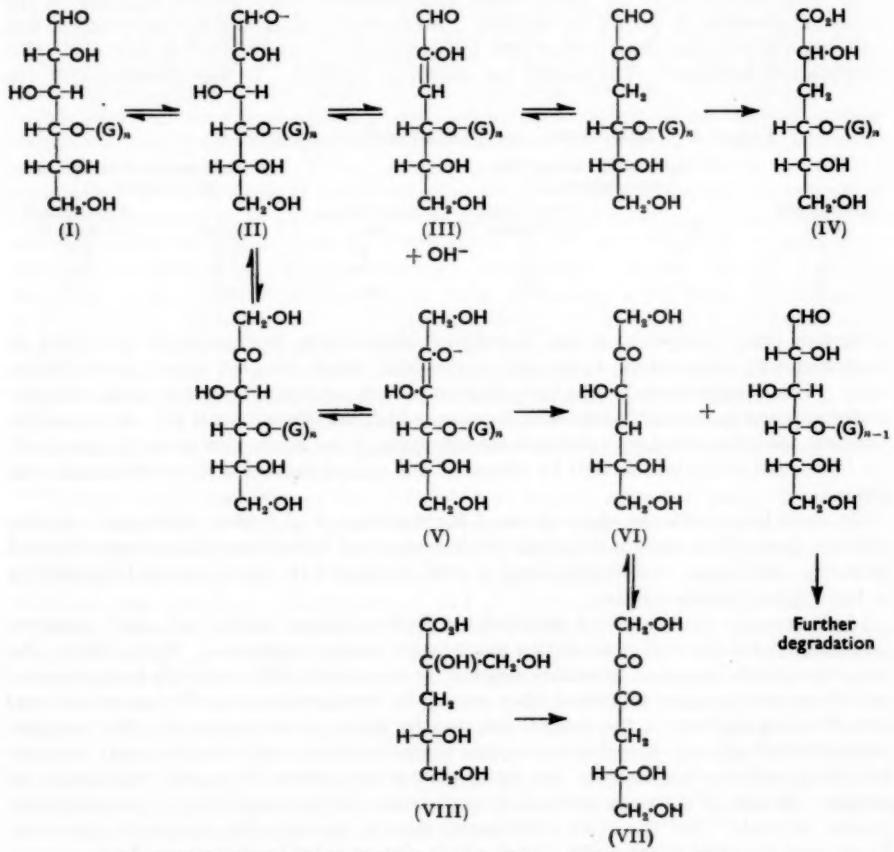
A large-scale hydrolysis of alkali-stable hydrocellulose yielded an acidic solution containing the stable end-group with a much larger amount of glucose. Hydrochloric acid was conveniently removed from this solution by treatment with methyldi-*n*-octylamine,[9] and the remaining acids separated from glucose by sorption on a suitable anion-exchange resin.[10] Examination of the neutral solution by paper chromatography, after enzymic destruction of glucose, revealed no neutral products other than cellobiose and traces of 5-hydroxymethylfurfuraldehyde, the latter presumably arising by acidic degradation of glucose. Elution of the acidic products from the resin, and examination by paper chromatography, indicated that the main constituents were α- and β-D-gluco*meta*saccharinic acid. There were traces of other acids, one of which corresponded on the paper chromatogram to α-D-glucosaccharinic acid. Pure α- and β-D-gluco*meta*saccharinic acid were isolated in the form of their lactones by preparative paper chromatography and identified as

[7] Rogovin, Konkin, and Rymashevskaya, *Khim. i Fiz. Khim. Vysokomolecul. Soedinenii Dokhady 7-oi Konf. Vysokomolecul. Soedineniyam*, 1952, 140; *Chem. Abs.*, 1954, **48**, 4449.
[8] Cf. Davidson and Nevell, *J. Textile Inst.*, in the press.
[9] Smith and Page, *J. Soc. Chem. Ind.*, 1948, **67**, 48.
[10] Machell, *J.*, 1957, 3389.

alkaloid salts. Hydrolysis of the original hydrocellulose in this way did not afford any acidic products, but did give the neutral compounds mentioned above.

It is concluded that during the degradation of cellulose by oxygen-free alkali, two types of competing reaction occur, which may be referred to as " degradation " and " stopping " reactions. Degradation reactions have been discussed earlier (Part I), and of these the most important are those leading to D-gluco*iso*saccharinic acid (VIII). The scheme indicates the predominant " degradation " and " stopping " reactions in terms of recent theories [11] of saccharinic acid formation.

The " stopping " reaction (I ⟶ IV) occurs at a much slower overall rate than the degradation (I ⟶ VIII), chiefly owing to the mass-law effect in reactions (II) ⟶ (III), and (V) ⟶ (VI).[12] Thus there is considerable degradation of a given cellulose molecule before the " stopping " reaction renders it stable.

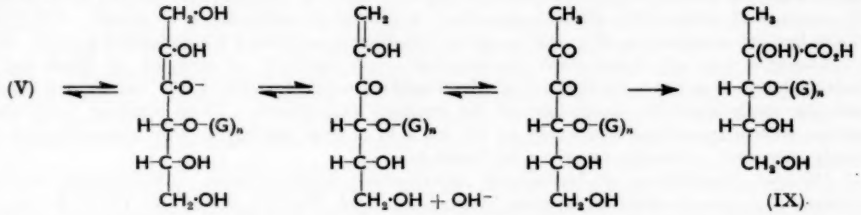


(I) = cellulose molecule of D.P. (n + 1). (IV) = alkali-stable residue.

The tentative identification of traces of α-D-glucosaccharinic acid [IX; H in place of $(G)_n$] in the hydrolysis products from the alkali-stable residue is in accord with the fact that the same saccharinic acid is a major product of the alkaline degradation of glucose.

[11] Kenner, *Chem. and Ind.*, 1955, 727, and references therein.
[12] Kenner and Richards, *J.*, 1957, 3019.

This sequence of reactions, however, is presumably less effective in the present instance than that resulting in formation of the *meta*-isomer (I ⟶ IV) owing to the fact that it involves a reactive intermediate (V) which can more readily break down by an alternate route (to VIII).



It is true that the D-gluco*meta*saccharinic acid end-group could have originated alternatively at a branch-chain of any length which was attached to the 3-position of a glucose unit in the main cellulose chain (compare, *e.g.*, the alkaline degradation of laminarin [13]), if this type of branch unit or chain were either present in the original cellulose or produced by acid reversion during preparation of the hydrocellulose.[14] While this cannot at present be disproved, it is regarded, on the evidence available at present, as unlikely to have an important effect on the " stopping reaction."

Experimental

The following solvents and sprays were used for paper chromatography with Whatman No. 1 paper at 25°: solvents *a*, butanol–pyridine–water (6 : 2 : 3); *b*, ethyl acetate–acetic acid–water [15] (10 : 1·3 : 1); *c*, butanol–ethanol–acetic acid–water (45 : 5 : 1 : 49); *d*, phenol–water (4 : 1). Sprays were: *a*, silver nitrate–sodium hydroxide; [16] *b*, hydroxylamine–ferric chloride; [17] *c*, B.D.H. 4·5 indicator; [18] *d*, buffered methyl-red.[19]

Degree of polymerisation (D.P.) of cellulose samples was determined by measurement of the viscosity of solutions of the nitrates in butyl acetate,[20] and methylene-blue absorption by Davidson's method.[21]

Acidity of solutions containing lactonisable acids was determined by adding a 2—4-fold excess of alkali and titrating the whole with acid to pH 9 after 30 min. at room temperature.

Preparation of Hydrocellulose.—American cotton, in the form of card sliver, was dewaxed by extraction (Soxhlet) with chloroform, followed by 95% ethanol, each for 18 hr. Initially, the acidic hydrolysis of the cotton to hydrocellulose was carried out with 2N-sulphuric acid for 6 hr. at 100°, but this gave material which probably contained ·O·SO_3H groups and was therefore abandoned.

Dewaxed cotton (100 g.) was then hydrolysed with 2N-hydrochloric acid (3 l.) for 5½ hr. at 100°, and then in a similar batch of fresh acid for a further 30 min. to hydrolyse any reversion products from the hydrocellulose. The product (80 g.) had a methylene-blue absorption of 0·38 mmoles/100 g., which accords with the results of other workers.[21] The hydrolysis was attended by a decrease in D.P. of the cellulose, from 4600 to 150. This hydrocellulose was used in all subsequent work.

For comparison, a portion of the original cotton was " scoured " by 0·5N-sodium hydroxide at 100° for 24 hr. in the absence of oxygen. The product was washed free from alkali, and then hydrolysed with 2N-hydrochloric acid at 100° for 6 hr. to give a hydrocellulose of methylene-blue absorption 0·22 mmole/100 g.

[13] Corbett and Kenner, *J.*, 1955, 1431.
[14] Sharples, unpublished work.
[15] Moilanen and Richtzenhain, *Acta Chem. Scand.*, 1954, **8**, 704.
[16] Trevelyan, Procter, and Harrison, *Nature*, 1950, **166**, 444.
[17] Abdel-Akher and Smith, *J. Amer. Chem. Soc.*, 1951, **73**, 5859.
[18] Nair and Muthe, *Naturwiss.*, 1956, **43**, 106.
[19] S. N. Parikh, J. M. Parikh, and Godbole, *Current Sci.*, 1954, **23**, 53.
[20] Harland, *J. Textile Inst.*, 1955, **46**, T483, and earlier references.
[21] Davidson, *ibid.*, 1948, **39**, T65.

Alkaline Degradation of Hydrocellulose.—Hydrocellulose (50 g.) was dried to constant wt. over phosphoric oxide at 0·1 mm., then suspended in water (750 ml.) through which oxygen-free nitrogen was passed. Oxygen-free N-sodium hydroxide (750 ml.) was added and the mixture heated at 100° in an atmosphere of nitrogen for 20 hr. After external cooling with ice, the residue was filtered off through sintered glass (porosity 4), washed successively with water, 1% acetic acid, water, 95% ethanol, and ether, and dried to constant wt. as above. The yield of alkali-stable residue was 21 g. (42%), methylene-blue absorption 4·2 mmoles/100 g., D.P. 180.

Acid-hydrolysis of Alkali-stable Hydrocellulose.—A number of samples of alkali-stable hydrocellulose (2 g.) were hydrolysed in N-hydrochloric acid (100 ml.) at 100° for varying times, and the methylene-blue absorption of the residues determined. These residues were then shaken with 0·1N-sodium hydroxide at 20° for 1 hr.; their methylene-blue absorptions were barely increased. Results are given in Table 1.

Alkaline Degradation of Hydrolysed Alkali-stable Hydrocellulose.—Alkali-stable hydrocellulose (5 g.) was hydrolysed with 2N-hydrochloric acid (250 ml.) at 100° for 18 hr., leaving a residue (4·1 g.) of methylene-blue absorption 1·0 mmole/100 g. A portion (3·2 g.) of this was degraded in 0·5N-sodium hydroxide at 100° for 20 hr. in the absence of oxygen, and the alkali-stable residue (1·47 g., 46%) recovered as before.

Hydrolysis of Alkali-stable Hydrocellulose and Isolation of the Soluble Products.—Alkali-stable hydrocellulose (50 g.), prepared as indicated above, was dialysed for several days to ensure complete removal of water-soluble acidic degradation products. The material had a yellow colour, which was completely removed by extraction (Soxhlet) with ethanol for 24 hr. The ultraviolet absorption spectrum of the extract had a peak 2700 Å. Concentration of the extract produced a gelatinous precipitate on which the chromatophore appeared to be adsorbed, and attempts to extract it from this residue by ether were unsuccessful. The extracted alkali-stable hydrocellulose was hydrolysed in N-hydrochloric acid (500 ml.) at 100° for 2 hr., and the residue separated and washed with water (1 l.) at 70°. After decolorisation with charcoal and cooling, about 98% of the mineral acid was removed from the combined filtrate and washings by Smith and Page's method,[9] *i.e.*, shaking the aqueous solution with methyl di-*n*-octylamine (128 g.) in chloroform (1400 ml.) and separating the layers. The aqueous layer was evaporated to about 200 ml. and slowly run through a column (0·8 cm. diam.) packed with washed Amberlite resin IR-120(H) (20 ml.) to remove cations. The effluent contained chloride which was precipitated by silver carbonate. After filtration, silver ions in solution were removed by passage through Amberlite resin IR-120(H) (20 ml.). A slightly acidic (pH 4) solution resulted, and a small portion of the solution was concentrated for paper chromatography.

Solvent *a* with spray *a*, and solvent *b* with spray *b*, revealed much glucose and a smaller amount of an acid lactone. The latter gave a diffuse spot of R_F *ca.* 0·35, and there was extensive " streaking " due to overloading of the glucose.

The main bulk of the solution was then separated into neutral and acidic fractions by using De-Acidite FF (micro-bead, 2% cross-linked) in the carbonate form.[10] This resin (5 g.) was stirred with the concentrated hydrolysate (50 ml.) for 24 hr. and the resin then transferred to a narrow column and washed with water (500 ml.). The filtrate and the initial washings (200 ml.) containing the neutral products were retained (see below).

After passage of " AnalaR " N-ammonium carbonate (100 ml.) through the resin, elution of acid was complete. The excess of ammonium carbonate in the effluent was decomposed by evaporation under reduced pressure, and the diluted residue (50 ml.) of ammonium salts passed through washed Amberlite resin IR-120(H) (10 ml.) to regenerate the free acids. Back-titration after treatment with excess of alkali, as above, indicated 0·44 meq. of acid.

In the same way, hydrolysis of the original hydrocellulose (50 g.) gave a neutral (see below) and an acidic fraction. The latter contained 0·13 meq. of acid and gave positive tests for hydrochloric and sulphuric acid, which arose from the reagents and ion-exchange resins. Paper chromatography of the acidic solution established the absence of the organic acids detected below. Therefore, by subtraction of this figure from the amount of acid isolated from the alkali-stable hydrocellulose, the true yield of acid peculiar to the latter should be 0·31 meq.

Identification of the Acid obtained by Hydrolysis of Alkali-stable Hydrocellulose.—Paper chromatography of the acid obtained as above, by using solvent *b* and spray *b*, revealed two main lactone spots of roughly equal intensity (R_F 0·33 and 0·38). In addition, there were traces of lactones with R_F 0·46, 0·53, and 0·70. β- and α-D-Gluco*meta*saccharinolactone and α-D-saccharinolactone had R_F 0·32, 0·37, and 0·52 respectively. Application of spray *a* to a

second chromatogram established the absence of glucose and the presence of small amounts of materials of R_F 0·10 and 0·21: only the former gave an acid reaction on the chromatogram with spray *c*. Conclusive identification of these products, in particular the two main lactones, depended on their prior separation, which was effected by large-scale paper chromatography.

To establish the feasibility of this approach, and to assess the efficiency of recovery, an attempt was made to separate in this way the authentic α- and β-D-gluco*meta*saccharinolactone. A solution of comparable amounts of these lactones with some free acids was obtained by treating a solution of the appropriate calcium salts with excess of Amberlite IR-120(H) resin. The lactone–acid mixture (1·60 meq., 0·259 g. calc. as lactone) was then transferred to a single sheet 22 × 24 in. of Whatman No. 3 MM. paper, which had been previously irrigated with the developing solvent for 2 days, and dried. After development in solvent *b* for 16 hr. the positions of the two lactones were determined by the application of spray *b* to indicator strips: the two lactones were almost separated. The horizontal strips bearing the two lactones, a 1 cm. wide mixed fraction between them, and the section containing the slower-moving free acids, were separately eluted with water. Paper chromatography of the two lactone fractions as above showed that both lactones were free from contamination with the anomer. Titration of aliquot portions of the eluted fractions as described above indicated a recovery of 47% in the combined lactone fractions, and a further 13% in the acidic eluate.

The acidic solution isolated from alkali-stable hydrocellulose was then transferred to No. 3 MM. paper and separated as above. The acidic material of R_F 0·10 was re-chromatographed in solvent *b*, and with spray *b* gave lactone spots corresponding to α- and β-D-gluco*meta*saccharinolactones as well as the spot due to the free acids (spray *c*). The material of R_F 0·21 was divided into two parts which were heated with N-hydrochloric acid and N-sodium hydroxide severally at 100° for 1 hr. Recovery of the organic products, followed by chromatography in solvent *b*, showed that these treatments were without effect on the material. This product was not investigated further.

Paper chromatography of the two main lactone fractions (A and B) from the above separation showed them to be pure, and their R_F values were compared with those of a number of authentic lactones, with solvents *b* and *c* and spray *b*. Details are shown in Table 3.

TABLE 3.

	Solvent *b*		Solvent *c*	
	R_F	R_S *	R_F	R_S *
D-Glucono-δ-lactone	0·27	0·53	0·32	0·63
β-D-Gluco*meta*saccharinolactone	0·32	0·62	0·32 †	0·64
Lactone A	0·32	0·61	0·32	0·64
Lactone B	0·36	0·70	0·38	0·74
α-D-Gluco*meta*saccharinolactone	0·37	0·72	0·38 †	0·75
α-D-Gluco*iso*saccharinolactone	0·39	0·76	0·43	0·85
α-D-Glucosaccharinolactone	0·52	1·0	0·51	1·0

* S = α-D-glucosaccharinolactone.
† In an earlier communication [23] these values were transposed in error.

Evaporation of the aqueous solutions of lactones A and B gave dried residues of 37 mg. and 34 mg. respectively. These proved to be contaminated with hemicellulose extracted from the chromatography paper. There was insufficient of each lactone present to permit exact determination by titration, but, on the basis of the results of previous experiments, the amounts of the α- and β-forms were probably of the order of 15 mg. and 20 mg. respectively.

β-D-*Gluco*meta*saccharinolactone*.—The residue (A) was extracted with acetone–ether (1 : 4), the solvent removed, and the residue taken up in ethyl acetate. The syrup obtained on evaporation did not crystallise: it was heated in water (5 ml.) with excess of strychnine at 100° for 4 hr. After cooling, the unchanged alkaloid was extracted with chloroform (4 × 10 ml.), and the solution evaporated to dryness at 40°/20 mm. The residue crystallised from absolute ethanol, then sintering and decomposing at 180—185° (Nef [23] gives decomp. 180—190° for strychnine β-D-gluco*meta*saccharinate).

α-D-*Gluco*meta*saccharinolactone*.—The lactone (B) was freed from hemicellulose as above, but did not crystallise. One portion was converted as above into the strychnine salt, m. p.

[22] Kenner and Richards, *J.*, 1954, 1784.
[23] Nef, *Annalen*, 1910, **376**, 1.

145—148° (Nef [23] gives m. p. 145—147° for strychnine α-D-gluco*meta*saccharinate). The brucine salt had m. p. 143—145°, alone or mixed with brucine α-D-gluco*meta*saccharinate.

Neutral Products from the Hydrolysis of Hydrocellulose and Alkali-stable Hydrocellulose.—In each case the aqueous solution of the neutral products (1·7 g. from alkali-stable hydrocellulose) obtained as described above was diluted to 250 ml. An aliquot portion (50 ml.) of each solution was diluted to 200 ml. and incubated with a glucose dehydrogenase preparation ("DeeO," kindly supplied by Takamine Laboratory, Inc., New Jersey, U.S.A.) (*ca.* 10 mg.) for 18 hr. at 35° in a stream of oxygen. In both cases, complete oxidation of the glucose to gluconic acid was achieved, and the acid was removed completely by stirring the concentrated solution (50 ml.) with De-Acidite FF (micro-bead, 2% cross-linked) (5 g.) in the carbonate form. Paper chromatography of the residual solutions, with solvent *d*, established the absence of glucose (R_F 0·41), and the presence of cellobiose, R_F 0·34, and traces of a second component, R_F 0·92, in both cases. The ultraviolet spectrum of both solutions showed max. at 2850 Å, with min. at 2450 Å, which are characteristic of 5-hydroxymethylfurfuraldehyde.[24] Application of spray *d* failed to detect any sorbitol (R_F 0·51) in either solution. In a separate experiment, it was shown that the glucose dehydrogenase had no measurable effect on an aqueous solution of sorbitol.

The authors are grateful to Dr. G. F. Davidson of the British Cotton Industry Research Association and to Dr. A. Sharples for helpful discussion. The former kindly arranged for the supply of cotton used in this work and the latter was responsible for the D.P. determinations. This work forms part of the programme of fundamental research undertaken by the Council of the British Rayon Research Association.

British Rayon Research Association, Heald Green Laboratories,
Wythenshawe, Manchester, 22. [*Received, June 11th,* 1957.]

[24] Wolfrom, Schuetz, and Cavalieri, *J. Amer. Chem. Soc.*, 1948, **70**, 514; Love, *Biochem. J.*, 1953, **55**, 126.

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907. *Heterocyclic Systems Related to Pyrrocoline. Part II.*[1] *The Preparation of Polyazaindenes by Dehydrogenative Cyclisations.*

By J. D. Bower and G. R. Ramage.

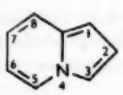
Some heterocyclic systems based on pyrrocoline (I), but having additional nitrogen atoms in the five-membered ring, have been prepared by dehydrogenation of pyridine derivatives.

In Part I [1] the preparation was described of 2 : 3*a*-diazaindene, one of the heterocyclic systems formally to be obtained by replacing =CH– groups of the five-membered ring of pyrrocoline (I) by nitrogen atoms. Three other, previously unknown systems of this class, namely 1 : 2 : 7*a*- and 1 : 3 : 3*a*-triazaindene and 1 : 7*a*-diazaindene (II, III, and IV respectively; R = H in each case) have now been prepared. These have in common a nitrogen atom at the 3-position of pyrrocoline (I), and cyclisation to form the five-membered ring was conveniently effected by dehydrogenation of suitably substituted pyridine derivatives so that a N–N bond was formed with the ring-nitrogen atom.

1 : 2 : 7*a*-Triazaindene (II; R = H) and its 3-methyl derivative (II; R = Me) were prepared by oxidation of the hydrazones (V; R = H and Me respectively) obtained by the action of hydrazine hydrate on pyridine-2-aldehyde and methyl 2-pyridyl ketone respectively. Distillation of the crude hydrazone (V; R = H) gave a residue of pyridine-2-aldazine (VI; R = H) which was also formed by the action of pyridine-2-aldehyde on the hydrazone. Methyl 2-pyridyl ketone hydrazone (V; R = Me) similarly reacted with the parent ketone and gave the azine (VI; R = Me). The azines were also formed as by-products during the oxidation of the hydrazones (V; R = H and Me) by alkaline

[1] Part I, Bower and Ramage, *J.*, 1955, 2834.

potassium ferricyanide, but the cyclisations proceeded readily and gave good yields of 1 : 2 : 7*a*-triazaindene (II; R = H) and its 3-methyl derivative (II; R = Me) respectively. These products were obtained as water-soluble, crystalline materials which exhibited a blue fluorescence in ultraviolet light. Methiodides were readily formed and silver nitrate



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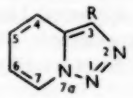

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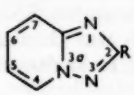

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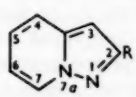

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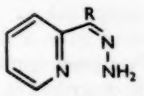
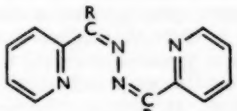


(V)

combined in equimolecular proportions to form complexes. Fargher and Furness [2] found that 1 : 2 : 3*a*-triazaindene formed a similar type of complex, whereas two moles of 2 : 3*a*-diazaindene combine with one mole of silver nitrate (Part I).[1]



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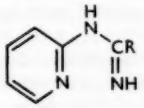

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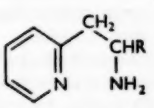

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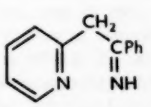

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Since this work was completed, Boyer, Borgers, and Wolford [3] have reported the preparation of the compounds (II; R = H and Ph) by the oxidation of the appropriate hydrazones by silver oxide.

Derivatives of 1 : 3 : 3*a*-triazaindenes (III) were prepared by the dehydrogenation of *N*-2-pyridylamidines (VII). The three substituted triazaindenes (III; R = Me, Ph, and *p*-tolyl) were prepared from the corresponding amidines (VII) which were obtained by the method of Oxley, Partridge, and Short [4] who prepared *N*-2-pyridylbenzamidine (VII; R = Ph) by the reaction of benzonitrile with 2-aminopyridine in the presence of aluminium chloride. The amidine (VII; R = Ph or *p*-tolyl) was readily cyclised by lead tetra-acetate in boiling acetic acid, and the products were obtained on dilution with water. It was more convenient to cyclise *N*-2-pyridylacetamidine (VII; R = Me) in boiling benzene since the product was very soluble in water, differing in this respect from the aryl-substituted compounds. Since the amidine (VII; R = H) has not yet been prepared, the parent member (III; R = H) was not obtained.

After several projected syntheses had been unsuccessful, the 1 : 7*a*-diazaindenes (IV; R = H and Ph) were obtained in reasonable yield from the amines (VIII; R = H and Ph respectively) by ferricyanide oxidation. The amine (VIII; R = Ph) was prepared by reduction of 2-phenacylpyridine oxime. Evidence supporting structure (IV; R = H) for the parent compound was provided by a molecular-weight determination and the formation of pyrazole-3-carboxylic acid on oxidation of the diazaindene by potassium permanganate. The ultraviolet absorption spectra of this and other polyazaindene systems afforded evidence confirming the structures of the new systems and this work is given in the following paper.

In the dehydrogenative cyclisations both the triazaindene systems were prepared by removal of the two hydrogen atoms. Several analogous cyclisations have been described, *e.g.*, the formation of 2 : 5-diphenyl-1 : 3 : 4-oxadiazole by ferricyanide oxidation of benzaldehyde benzoylhydrazone [5] and the preparation of benziminazoles and benzoxazoles

[2] Fargher and Furness, *J.*, 1915, **107**, 688.
[3] Boyer, Borgers, and Wolford, *J. Amer. Chem. Soc.*, 1957, **79**, 678.
[4] Oxley, Partridge, and Short, *J.*, 1947, 1110.
[5] Stollé and Münch, *J. prakt. Chem.*, 1904, **70**, 393.

by lead tetra-acetate oxidation of Schiff's bases from *o*-diamines and *o*-aminophenols respectively.[6]

The formation of the 1 : 7*a*-diazaindene system, however, differs in that four hydrogen atoms were removed. That this did not proceed through the imine [7] (by the removal of two hydrogen atoms) and a subsequent cyclisation of the type discussed above was suggested by the failure to cyclise the imine (IX). It appeared likely that cyclisation first gave a dihydro-compound which was then dehydrogenated. A similar procedure has been applied to the preparation of 1 : 3*a*-diazaindene from its dihydro-derivative and is described in the following paper.

Experimental

Pyridine-2-aldehyde Hydrazone (V; R = H).—Pyridine-2-aldehyde (5·0 g.) and 90% hydrazine hydrate (10 c.c.) were heated together at 90—100° for 30 min. 30% Sodium hydroxide solution (10 c.c.) was added to the cooled solution which was then extracted with ether. The extract was dried (KOH) and fractionation gave the crude hydrazone (4·3 g.), b. p. 124—128°/5 mm., as a pale yellow liquid which, on redistillation, gave *pyridine-2-aldehyde hydrazone*, b. p. 127°/5 mm. (Found: C, 59·7; H, 6·0; N, 34·2. $C_6H_7N_3$ requires C, 59·5; H, 5·8; N, 34·7%). *Pyridine-2-aldehyde 4-phenylthiosemicarbazone*, prepared from the hydrazone and phenyl *iso*thiocyanate in boiling benzene, formed felted needles, m. p. 191—192°, from methanol (Found: C, 60·7; H, 4·4. $C_{13}H_{12}N_4S$ requires C, 60·9; H, 4·7%). The residue from the first distillation of the hydrazone, the *aldazine* (VI; R = H), crystallised from ethanol as yellow plates, m. p. 152° (Found: C, 69·0; H, 5·0. $C_{12}H_{10}N_4$ requires C, 68·6; H, 4·8%), and was also prepared from the hydrazone by reaction with pyridine-2-aldehyde.

Methyl 2-Pyridyl Ketone Hydrazone (V; R = Me).—Methyl 2-pyridyl ketone (5·0 g.) and 100% hydrazine hydrate (8 c.c.) were heated at 90—100° for 2½ hr. The cooled solution deposited a solid which was removed and combined with the material obtained by extraction with ether. Crystallisation of the product (5·5 g.) from benzene–light petroleum (b. p. 60—80°) gave the *hydrazone* as needles, m. p. 77—78° (Found: C, 62·1; H, 6·45. $C_7H_9N_3$ requires C, 62·2; H, 6·7%). *Methyl 2-pyridyl ketone 4-phenylthiosemicarbazone* formed very pale yellow needles, 178—179°, from ethanol (Found: C, 61·9; H, 5·05. $C_{14}H_{14}N_4S$ requires C, 62·2; H, 5·2%).

1 : 2 : 7a-*Triazaindene* (II; R = H).—Pyridine-2-aldehyde hydrazone (5·7 g.), potassium ferricyanide (33·5 g.), sodium hydrogen carbonate (8·6 g.), and water (220 c.c.) were heated together at 90—100° for 45 min. The solid azine (1·6 g.) was removed and 30% sodium hydroxide solution (20 c.c.) was added to the filtrate which was then extracted with chloroform. Distillation of the extract gave a fraction (2·9 g., 51%), b. p. 142—145°/7 mm., which solidified. Chromatography on alumina in a 1% solution of methanol in benzene, followed by evaporation at 110°/4 mm. on to a " cold-finger " condenser, gave 1 : 2 : 7a-*triazaindene* as prisms, m. p. 39—40° (Found: C, 60·2; H, 4·3. $C_6H_5N_3$ requires C, 60·5; H, 4·2%). The *methiodide* formed plates, m. p. 176°, from propanol (Found: C, 32·2; H, 3·3. $C_7H_8N_3I$ requires C, 32·2; H, 3·1%), and the 1 : 1 *compound* with silver nitrate was obtained as needles, m. p. 136° (decomp.), from very dilute nitric acid (Found: C, 25·5; H, 2·1. $C_6H_5N_3,AgNO_3$ requires C, 24·9; H, 1·7%).

3-*Methyl*-1 : 2 : 7a-*triazaindene* (II; R = Me).—Potassium ferricyanide (18·8 g.) and sodium hydrogen carbonate (4·9 g.) in water (150 c.c.) were added to methyl 2-pyridyl ketone hydrazone (3·5 g.). The mixture was heated at 90—100° for 30 min. to complete the reaction, which began at once. Filtration of the cooled mixture gave *methyl 2-pyridyl ketazine* (VI; R = Me) (0·1 g.) which formed yellow needles, m. p. 54°, on crystallisation from aqueous methanol (Found: C, 70·3; H, 6·0. $C_{14}H_{14}N_4$ requires C, 70·6; H, 5·9%). The filtrate was basified and extracted with chloroform. Fractionation of the extract gave an oil (2·75 g., 79%), b. p. 116—120°/2 mm., which soon solidified and was crystallised from benzene–light petroleum (b. p. 60—80°) and then evaporated at 100°/2 mm. on to a " cold-finger " condenser. 3-*Methyl*-1 : 2 : 7a-*triazaindene* was obtained as needles, m. p. 84—85°, which had a faint deep blue fluorescence under ultraviolet light (Found: C, 62·9; H, 5·0. $C_7H_7N_3$ requires C, 63·1; H,

[6] Stephens, *Nature*, 1949, **164**, 342; Stephens and Bower, *J.*, 1949, 2971; 1950, 1722.
[7] Wibaut and de Jong, *Rec. Trav. chim.*, 1949, **68**, 485.

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5·3%). The 1 : 1 *compound* with silver nitrate crystallised from water as needles, m. p. 195° (decomp.) (Found: C, 28·5; H, 2·2. $C_7H_7N_3,AgNO_3$ requires C, 27·7; H, 2·3%).

N-2-*Pyridylacetamidine* (VII; R = Me).—Aluminium chloride (7·5 g.) was added to a mixture of 2-aminopyridine (4·7 g.) and acetonitrile (3·3 g.). After the vigorous reaction had subsided the mixture was heated at 200° (bath) for 15 min., cooled, and decomposed with water (25 c.c.), and neutral material was removed by ether. The aqueous solution was then made strongly alkaline and extracted with ether.

The extracts from four such experiments were combined, dried (Na_2SO_4), and on fractionation gave 2-aminopyridine (5·2 g., 27%) followed by the crude amidine (11·9 g., 44% on initial aminopyridine), b. p. 126—127°/3 mm., which solidified. This was sufficiently pure for conversion into the triazaindene, but a sample was purified by chromatography on alumina in benzene containing 1% of ethanol. After a yellow impurity had passed through, the product was eluted with ethanol and evaporation twice over phosphoric oxide at 80°/2 mm. gave *N*-2-pyridylacetamidine as deliquescent prisms, m. p. 67—68°. The *picrate* formed felted yellow needles, m. p. 188—189°, from methanol (Found: C, 42·7; H, 3·1. $C_7H_9N_3,C_6H_3O_7N_3$ requires C, 42·9; H, 3·3%). The derivative with phenyl *iso*thiocyanate, *N-phenyl-N'-(N-2-pyridylacetimidoyl)thiourea*, formed needles, m. p. 134°, from benzene (Found: C, 62·2; H, 4·8. $C_{14}H_{14}N_4S$ requires C, 62·2; H, 5·2%).

N-2-*Pyridyl*-p-*toluamidine* (VII; R = *p*-tolyl).—The process used to prepare *N*-2-pyridylbenzamidine [4] was applied to *p*-tolunitrile and gave N-2-*pyridyl*-p-*toluamidine* (53%), which crystallised from light petroleum (b. p. 60—80°) as needles, m. p. 127° (Found: C, 73·9; H, 6·2. $C_{13}H_{13}N_3$ requires C, 73·9; H, 6·2%).

2-*Methyl*-1 : 3 : 3a-*triazaindene* (III; R = Me).—*N*-2-Pyridylacetamidine (2·2 g.) was heated under reflux in benzene (25 c.c.) with lead tetra-acetate (7·4 g.) for 30 min. The cooled, filtered solution was extracted with 30% sodium hydroxide solution, and the organic layer was separated and distilled. A fraction (1·7 g., 78%), b. p. 130—135°/27 mm., which solidified, was redistilled (b. p. 137°/32 mm.) and evaporated at 70°/3 mm. on to a " cold-finger " condenser and gave 2-*methyl*-1 : 3 : 3a-*triazaindene* as deliquescent prisms, m. p. 49—50° (Found: C, 63·0; H, 5·7. $C_7H_7N_3$ requires C, 63·1; H, 5·3%). The *picrate* formed prisms, m. p. 177—178°, from methanol (Found: C, 43·0; H, 2·8. $C_7H_7N_3,C_6H_3O_7N_3$ requires C, 43·1; H, 2·8%).

2-*Phenyl* 1 : 3 : 3a-*triazaindene* (III; R = Ph).—Lead tetra-acetate (4·4 g.) and *N*-2-pyridylbenzamidine [4] (1·97 g.) were boiled for 10 min. in acetic acid (15 c.c.), and the solution was then poured into water. The dried precipitate was crystallised from light petroleum (b. p. 40—60°), and the resulting crystals (1·25 g.), m. p. 139°, were purified by evaporation at 150°/2 mm., followed by chromatography on alumina in benzene–ethanol (95 : 5 v/v). Further crystallisation gave 2-*phenyl*-1 : 3 : 3a-*triazaindene* as prisms, m. p. 141° (Found: C, 73·7; H, 4·6. $C_{12}H_9N_3$ requires C, 73·8; H, 4·6%). The *picrate* formed felted yellow needles, m. p. 168°, from ethanol (Found: C, 51·2; H, 3·6. $C_{12}H_9N_3,C_6H_3O_7N_3,C_2H_6O$ requires C, 51·1; H, 3·9%).

2-p-*Tolyl*-1 : 3 : 3a-*triazaindene* (III; R = *p*-tolyl).—A similar process to the above gave 2-p-*tolyl*-1 : 3 : 3a-*triazaindene* (60%) as needles, m. p. 173°, from aqueous ethanol (Found: C, 74·5; H, 5·2. $C_{13}H_{11}N_3$ requires C, 74·6; H, 5·3%).

2-(β-*Aminophenethyl*)*pyridine* (VIII; R = Ph).—Concentrated hydrochloric acid (30 c.c.) was added, in portions during about 5 min., to 2-phenacylpyridine oxime [8] (7·5 g.) and zinc (15·0 g.) in boiling methanol (200 c.c.). Boiling was continued for a further 10 min. before the mixture was filtered and the filtrate concentrated. A large excess of 30% sodium hydroxide solution was added and the product was isolated by ether. A fraction (4·5 g.), b. p. 157—162°/2 mm., on redistillation gave 2-(β-*aminophenethyl*)*pyridine* as a yellow oil, b. p. 160°/2 mm. (Found C, 79·2; H, 7·5. $C_{13}H_{14}N_2$ requires C, 78·8; H, 7·1%). The *picrate* formed prisms, m. p. 148°, from methanol (Found: C, 53·1; H, 4·1. $C_{13}H_{14}N_2,C_6H_3O_7N_3$ requires C, 53·4; H, 4·0%). The *benzoyl* derivative formed needles, m. p. 148°, from ligroin (Found: C, 78·8; H, 6·0. $C_{20}H_{18}ON_2$ requires C, 79·4; H, 6·0%).

1 : 7a-*Diazaindene* (IV; R = H).—Potassium ferricyanide (142 g.), sodium hydrogen carbonate (36·5 g.), and 2-2'-aminoethylpyridine [9] (12·8 g.) were heated in water (435 c.c.) at 90—100° for 4 hr. A 30% solution of sodium hydroxide (60 c.c.) was added to the cooled solution before extraction with chloroform. The material left on evaporation of the chloroform

[8] Scheuing and Winterhalder, G.P. 594,849.
[9] Kirchner, McCormick, Cavallito, and Miller, *J. Org. Chem.*, 1949, **14**, 388.

was extracted with benzene, and the benzene extract was concentrated and chromatographed on alumina. The fast-moving wide band, having a blue-violet fluorescence in ultraviolet light, was collected and gave, on distillation, 1 : 7a-*diazaindene* (2·6 g.), b. p. 108°/25 mm. [Found: C, 70·9; H, 5·3; N, 23·8%; *M* (cryoscopic, in benzene), 118. $C_7H_6N_2$ requires C, 71·2; H, 5·1; N, 23·7%; *M*, 118]. The *picrate* formed needles, m. p. 151° (decomp.), from ethanol and was dried over phosphoric oxide at 60°/2 mm. for 30 min. before analysis (Found: C, 45·6; H, 3·8. $C_7H_6N_2,C_6H_3O_7N_3,C_2H_6O$ requires C, 45·8; H, 3·8%).

Oxidation of the diazaindene (0·5 g.) in water (200 c.c.) at 50—55° with potassium permanganate (3·7 g.), filtration, and evaporation of the acidified filtrate to dryness, followed by extraction of the residue with acetone and evaporation gave pyrazole-3-carboxylic acid (0·15 g.), which crystallised from dilute hydrochloric acid as prisms, m. p. and mixed m. p. 211—212° (ethyl ester, m. p. and mixed m. p. 159—160°). The authentic sample of acid was prepared by the method of Pechmann and Burkard.[10]

2-*Phenyl*-1 : 7a-*diazaindene* (IV; R = Ph).—2-(β-Aminophenethyl)pyridine (1·5 g.), potassium ferricyanide (12·5 g.), and sodium hydrogen carbonate (3·2 g.) were heated at 90—100° in water (50 c.c.) for 3 hr. The cooled solution deposited a solid (1·3 g.) which, after several crystallisations from aqueous methanol, gave 2-*phenyl*-1 : 7a-*diazaindene* as needles, m. p. 109° (Found: C, 80·3; H, 5·2; N, 14·7. $C_{13}H_{10}N_2$ requires C, 80·4; H, 5·2; N, 14·4%).

The authors thank the Huddersfield Education Authority for the award of a Research Scholarship to one of them (J. D. B.), the Chemical Society for a grant from the Research Fund, and P. Naylor for technical assistance.

THE TECHNICAL COLLEGE, HUDDERSFIELD.
ROYAL TECHNICAL COLLEGE, SALFORD. [*Received, May 9th*, 1957.]

[10] Pechmann and Burkard, *Ber.*, 1900, **33**, 3594.

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908. *Heterocyclic Systems Related to Pyrrocoline. Part III.*[1] *The Ultraviolet Absorption of Some Polyazaindenes.*

By J. D. BOWER.

An improved synthesis of 1 : 3*a*-diazaindene (pyrimidazole) is described. The ultraviolet absorption spectra of the polyazaindene systems having the nitrogen atoms in the five-membered ring are recorded and compared.

THE preparation of several new polyazaindene systems was described in Parts I and II.[1] Spectroscopic confirmation of their structures is now presented. For this purpose the other polyazaindenes having the nitrogen atoms only in the five-membered ring have been prepared and the ultraviolet absorption spectra of all the systems have been examined. In general, standard methods were used for the preparation of the known compounds.

Kröhnke and his co-workers [2] recently reported investigations of routes to derivatives of 1 : 3*a*-diazaindene (pyrimidazole), but the only preparation of the parent member (I; R = H) so far is that by Tschitschibabin [3] who prepared it from bromoacetaldehyde and 2-aminopyridine in unstated yield. This compound is conveniently prepared by dehydrogenation of the readily available 2 : 3-dihydro-1 : 3*a*-diazaindene [4] by potassium ferricyanide or lead tetra-acetate.

1 : 2 : 3*a*-Triazaindene (II; R = H) was prepared by a slight modification of the published method,[5] and the 3-methyl derivative (II; R = Me) was also obtained. The hygroscopic nature of the former was confirmed, and the latter readily forms a hydrate.

Details of the ultraviolet absorption spectra (*cyclo*hexane solutions) of the parent

[1] Part I, Bower and Ramage, *J.*, 1955, 2834; Part II, *idem*, preceding paper.
[2] Schilling, Kröhnke, and Kickhöfen, *Chem. Ber.*, 1955, **88**, 1093; Kröhnke and Kickhöfen, *ibid.*, p. 1103.
[3] Tschitschibabin, *Ber.*, 1925, **58**, 1704.
[4] Bremer, *Annalen*, 1936, **521**, 286.
[5] Fargher and Furness, *J.*, 1915, 688.

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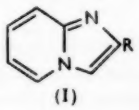
members of six of the seven polyazaindenes having the nitrogen atoms in the five-membered ring are given in the Table and Figures. The exception, 1 : 3 : 3*a*-triazaindene, has not yet been prepared, but details of the spectrum of its 2-methyl derivative are given. Since, in general, the presence of a *C*-methyl substituent has little effect on the spectrum of a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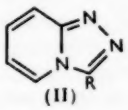
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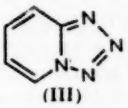
(III)

heterocyclic compound,[6] it is considered justifiable to regard the spectrum of 2-methyl-1 : 3 : 3*a*-triazaindene as being very similar to that of the parent in a comparative study of the forms of the spectra of the systems. The spectra of some phenylpolyazaindenes are also recorded.

Consideration of the compounds as derived from pyrrocoline shows a clear connection between the spectra and the number and positions of the nitrogen atoms. The spectrum

Ultraviolet absorption spectra.

Compound	M. p.	Concn. (10^{-5}M)	Absorption max. (Å) and log ε (in parentheses)							
Pyrrocoline [a]	74°	2·08	3815 (2·92)	3610 (3·24)	3465 (3·29)	3360 * (3·23)	2945 (3·56)	2825 (3·45)	2755 (3·34)	2375 (4·51)
1 : 3*a*-Diazaindene [b]	(109°/2 mm.†)	3·40	3360 (3·10)	3200 (3·38)	3100 (3·42)		2800 (3·41)	2725 (3·38)	2530 * (3·15)	2285 * (4·29)	2245 (4·41)
2 : 3*a*-Diazaindene [c]	54—55°	3·40	3785 (2·89)	3580 (3·20)	3440 (3·27)	3330 * (3·23)	2845 (3·66)	2735 (3·72)	2650 * (3·55)		2180 (4·46)
1 : 7*a*-Diazaindene [d]	(108°/25 mm.†)	3·22	3400 (2·72)	3230 * (3·14)	3100 (3·25)	3005 * (3·26)	2890 (3·52)	2810 * (3·46)		2270 (4·54)	2225 (4·56)
1 : 2 : 3*a*-Triazaindene (hydrate) [b]	36°	3·27	3260 (2·93)	3110 (3·28)	2990 (3·36)	2930 * (3·34)	2700 (3·33)	2595 (3·32)			2140 (4·35)
2-Methyl-1 : 3 : 3*a*-triazaindene [d]	49—50°	3·19	2940 * (3·20)	2810 * (3·52)			2730 (3·57)				2175 (4·58)
1 : 2 : 7*a*-Triazaindene [d]	39—40°	3·17	3355 (2·85)	3190 * (3·25)	3060 (3·34)	3000 (3·33)	2835 (3·66)	2740 (3·67)			2130 (4·38)
1 : 2 : 3 : 3*a*-Tetraazaindene [e]	157°	3·50	2930 (3·16)	2805 (3·47)			2685 * (3·61)	2645 (3·62)			<2100
2-Phenylpyrrocoline [f]	214°	1·97	3845 (3·15)	3660 (3·43)	3500 (3·45)	3250 * (3·27)			2545 (4·62)		
2-Phenyl-1 : 3*a*-diazaindene [g]	136°	1·82	3480 (3·67)	3325 (3·88)	3200 (3·85)		2950 (3·66)	2830 (3·69)	2480 (4·62)		
2-Phenyl-1 : 7*a*-diazaindene [d]	109°	1·87	3430 (2·80)	3260 * (3·26)			2685 (4·49)	2590 (4·56)	2440 (4·53)		
2-Phenyl-1 : 3 : 3*a*-triazaindene [d]	141°	1·77	3060 (3·58)	2925 * (3·73)	2810 * (3·88)			2525 (4·56)	2445 (4·56)		
3-Phenyl-2 : 3*a*-diazaindene [e]	109°	1·46		3180 (4·11)				2285 (4·22)			
3-Phenyl-1 : 2 : 3*a*-triazaindene [h]	176°	2·54		2875 (3·97)			2430 (4·16)	2210 (4·23)			

* Inflexion. † B. p.

Preparations: [a] By decarboxylation (Diels *et al.*, *Annalen*, 1932, **498**, 16) of pyrrocoline-2-carboxylic acid (Borrows and Holland, *J.*, 1947, 672). [b] See Experimental. [c] Part I. [d] Preceding paper. [e] Ref. 5. [f] Borrows, Holland, and Kenyon, *J.*, 1946, 1069. [g] Ref. 8. [h] Bower and Doyle, *J.*, 1957, 727.

of pyrrocoline (Fig. 1) consists of three absorption bands, the two at longer wavelengths showing characteristic fine structure. Replacement of the –CH= group in the 2-position by nitrogen, to give 2 : 3*a*-diazaindene (Fig. 1) causes a slight hypsochromic shift, but in the 1- or 3-position the effect, especially on the longest-wavelength band, is considerably

[6] See, *e.g.*, Ames, Bowman, and Grey, *J.*, 1953, 3008; Cookson, *ibid.*, p. 2789; Passerini, *J.*, 1954, 2256.

greater. The effect is cumulative with the introduction of further nitrogen atoms and results in the merging of the two long-wavelength bands into one in the spectrum of 1 : 2 : 3 : 3*a*-tetra-azaindene [5] (III) (Fig. 1), though some fine structure, characteristic of the long-wavelength band, is still visible.

In the spectra of 2- and 3-phenylpolyazaindenes (Fig. 2) the effects of introducing nitrogen are similar to those for parent compounds.

The relations between the spectra, reflecting the differences between the compounds in the number and position of the nitrogen atoms, are regarded as supporting the assignment, in Parts I and II, of structures to those polyazaindenes not previously described.

The spectra of the phenylpolyazaindenes provide further evidence about the structure

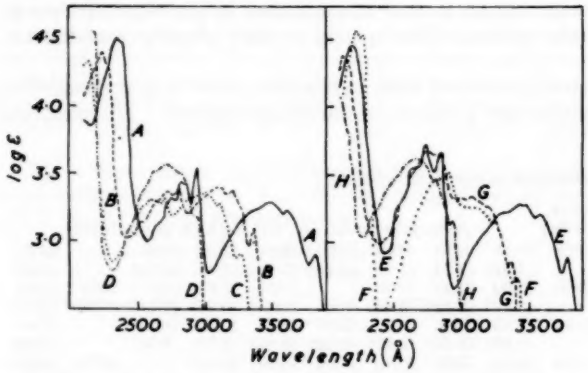

FIG. 1.

A, Pyrrocoline. B, 1 : 3a-*Diazaindene. C,* 1 : 2 : 3a-*Triazaindene hydrate. D,* 2-*Methyl*-1 : 3 : 3a-*triazaindene. E,* 2 : 3a-*Diazaindene. F,* 1 : 7a-*Diazaindene. G,* 1 : 2 : 7a-*Triazaindene. H,* 1 : 2 : 3 : 3a-*Tetra-azaindene.*

of the compound, m. p. 135—136°, obtained from the reaction of 2-aminopyridine with ω-bromoacetophenone. Tschitschibabin [7] and Schmid and Bangler [8] regarded this as 2-phenyl-1 : 3*a*-diazaindene (though without conclusive evidence), but Djerassi and Pettit [9] favoured the 3-phenyl structure. Recently Kröhnke, Kickhöfen, and Thoma [10] have shown that the compound is, in fact, the 2-phenyl isomer (I; R = Ph) and this is supported by the spectrum (Fig. 2), which is of the same type as those of 2-phenylpyrrocoline and 2-phenyl-1 : 3 : 3*a*-triazaindene but distinct from those of 3-phenyl-2 : 3*a*-diazaindene and 3-phenyl-1 : 2 : 3*a*-triazaindene. An isomer, m. p. 98°, considered to be 3-phenyl-1 : 3*a*-diazaindene has been described.[11]

EXPERIMENTAL

Absorption Spectra.—These were determined in *cyclo*hexane solution (for concentrations see Table) on a Unicam S.P. 500 spectrophotometer. 1 cm. and 4 cm. cells were used.

1 : 3a-*Diazaindene* (*Pyrimidazole*) (I; R = H).—(*a*) 2 : 3-Dihydro-1 : 3*a*-diazaindene [4] (4·65 g.), potassium ferricyanide (31·9 g.), and sodium hydrogen carbonate (8·2 g.) were heated in water (125 c.c.) at 90—100° for 30 min. Addition of 30% sodium hydroxide solution (25 c.c.), extraction with chloroform, and distillation of the dried (Na_2SO_4) extract gave a yellow oil (3·63 g., 79%), b. p. 114—115°/3 mm. The colour was removed by the passage of the oil, in benzene containing 1% by volume of ethanol, through a column of alumina, and 1 : 3*a*-diazaindene (2·76 g., 60%), b. p. 109°/2 mm., was obtained on distillation of the eluate (Found: C, 71·2; H, 5·1. Calc. for $C_7H_6N_2$: C, 71·2; H, 5·1%). It showed a blue fluorescence under ultraviolet light. The *picrate* formed fine needles, m. p. 205°, from ethanol (Found: C, 45·4;

[7] Tschitschibabin, *Ber.*, 1926, **59**, 2048.
[8] Schmid and Bangler, *ibid.*, p. 1360.
[9] Djerassi and Pettit, *J. Amer. Chem. Soc.*, 1954, **76**, 4470.
[10] Kröhnke, Kickhöfen, and Thoma, *Chem. Ber.*, 1955, **88**, 1117.
[11] Gol'dfarb and Kondakova, *J. Appl. Chem. U.S.S.R.*, 1942, **15**, 151.

H, 2·9. $C_7H_6N_2,C_6H_3O_7N_3$ requires C, 45·0; H, 2·6%), and the *methiodide* fine needles, m. p. 207°, from propanol (Found: C, 37·1; H, 3·7. $C_8H_9N_2I$ requires C, 36·9; H, 3·5%).

(*b*) Lead tetra-acetate (4·5 g.) was added to 2 : 3-dihydro-1 : 3*a*-diazaindene (1·2 g.) in benzene (50 c.c.). After complete reaction the mixture was filtered, the filtrate washed with 30% sodium hydroxide solution, and the benzene layer fractionated to give 1 : 3*a*-diazaindene (0·56 g., 47%), b. p. 115°/3 mm. The picrate was identical with that obtained by method (*a*).

1 : 2 : 3a-*Triazaindene* (II; R = H).—The procedure used was that of Fargher and Furness,[5] except that the distillation was continued after the removal of the excess of formic acid and the triazaindene (81%) was obtained as a liquid, b. p. 218°/6 mm., which formed a deliquescent solid. Crystallisation from moist benzene or moist ethyl acetate gave the *hydrate* as needles, m. p. 36° (Found: C, 52·4; H, 5·0. $C_6H_5N_3,H_2O$ requires C, 52·5; H, 5·1%).

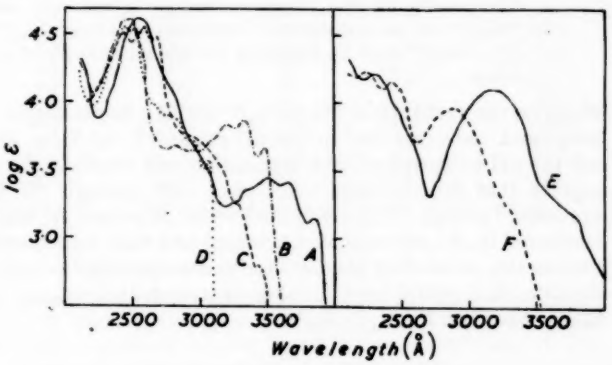

FIG. 2.

A, 2-Phenylpyrrocoline. B, 2-Phenyl-1 : 3a-diazaindene. C, 2-Phenyl-1 : 7a-diazaindene. D, 2-Phenyl-1 : 3 : 3a-triazaindene. E, 3-Phenyl-2 : 3a-diazaindene. F, 3-Phenyl-1 : 2 : 3a-triazaindene.

Although the hydrate could be partly dehydrated over phosphoric oxide an anhydrous sample was not obtained.

3-*Methyl*-1 : 2 : 3a-*triazaindene* (II; R = Me).—2-Pyridylhydrazine (2·0 g.) was boiled in acetic anhydride (4 c.c.) for 5 hr. The excess of solvent was removed under reduced pressure and the residue was treated with 30% sodium hydroxide solution (20 c.c.). The resulting solid was extracted with chloroform, the extract evaporated, and the residue crystallised from benzene to give 3-*methyl*-1 : 2 : 3a-*triazaindene* as prisms, m. p. 134° (Found: C, 62·5; H, 5·3. $C_7H_7N_3$ requires C, 63·1; H, 5·3%). The *trihydrate* formed needles, m. p. 56°, from water or moist ethyl acetate (Found: C, 45·6; H, 7·1. $C_7H_7N_3,3H_2O$ requires C, 44·9; H, 7·0%). The *picrate* formed prisms, m. p. 239—241°, from acetone (Found: C, 43·1; H, 3·1. $C_7H_7N_3,C_6H_3O_7N_3$ requires C, 43·1; H, 2·8%). The *methiodide*, obtained as needles, m. p. 243—244°, from acetone (Found: C, 34·8; H, 3·9. $C_8H_{10}N_3I$ requires C, 34·9; H, 3·7%), when boiled with *p*-dimethylaminobenzaldehyde in methanol containing a little piperidine, formed 3-p-*dimethylaminostyryl*-2-*methyl*-1 : 2 : 3a-*triazaindene iodide*, which crystallised from methanol as fine orange needles, m. p. 269° (Found: C, 50·3; H, 4·6. $C_{17}H_{19}N_4I$ requires C, 50·4; H, 4·7%), $\lambda_{max.}$ 4220 Å (ε 35,800; $1·1 \times 10^{-5}$M in MeOH).

The work was carried out during the tenure of a Huddersfield Education Committee Research Scholarship and with the help of a grant from the Chemical Society Research Fund. Thanks are offered to Dr. G. R. Ramage, F.R.I.C., for advice, to the Wool Textile Research Council for the loan of the spectrophotometer, and to P. Naylor for technical assistance.

THE TECHNICAL COLLEGE, HUDDERSFIELD. [*Received, May 9th*, 1957.]

909. *Exchange Studies of Certain Chelate Compounds of the Transitional Metals. Part IV.* The Rates of Dissociation of Bis- and Mono-(1 : 10-phenanthroline)nickel(II) Ion determined by* $^{63}Ni^{2+}$ *Exchange.*

By R. G. Wilkins and M. J. G. Williams.

The rate constants for dissociation of $[Ni\ phen_2]^{2+}$ and $[Ni\ phen]^{2+}$ have been determined from exchange experiments with ^{63}Ni. The values $10^{14}\exp(-23{,}100/RT)$ and $10^{16}\exp(-26{,}200/RT)$ respectively are compared with that of the $[Ni\ phen_3]^{2+}$ species, $10^{15\cdot2}\exp(-25{,}200/RT)$, obtained from previous [^{14}C]phenanthroline exchange studies (all values are in min.$^{-1}$). The results for the bisphenanthroline species are established by adding $^*Ni_{aq}^{2+}$ to an equilibrium mixture containing Ni_{aq}^{2+}, $[Ni\ phen]^{2+}$, and $[Ni\ phen_2]^{2+}$, and by following the specific activity of each species at various times.

Work on the exchange of $[Ni\ phen_3]^{2+}$ with 1 : 10-phenanthroline, [^{14}C]-labelled materials being used, indicated that in the pH range 5·7—11·7 the exchange rate constant (k_{exch}) and the pH-independent acid-dissociation rate constant (k_a) were identical.[1] This result requires that the exchange takes place only through the first dissociative equilibrium represented in eqn. (1) (co-ordinated water molecules are not included in the equations or considered in the subsequent discussion) and that subsequent stages do not assist in the introduction of labelled phenanthroline into the trisphenanthroline ion. If this were not the case, k_{exch} would have a value such that $3k_a \geqslant k_{exch} > k_a$ with the limiting case of $k_{exch} = 3k_a$ when $R_2, R_1 \gg R_3$.[2]

$$\left.\begin{aligned} [Ni\ phen_3]^{2+} &\underset{R_3}{\rightleftharpoons} [Ni\ phen_2]^{2+} + phen \ldots\ldots k_3, k_{-3} \\ [Ni\ phen_2]^{2+} &\underset{R_2}{\rightleftharpoons} [Ni\ phen]^{2+} + phen \ldots\ldots k_2, k_{-2} \\ [Ni\ phen]^{2+} &\underset{R_1}{\rightleftharpoons} Ni^{2+} + phen \ldots\ldots k_1, k_{-1} \end{aligned}\right\} \quad \ldots \quad (1)$$

Since the concentrations of the bis- and mono-phenanthrolinenickel(II) species will be very small under the conditions of ligand exchange with the tris-derivative, the value of k_2 and k_1 may still be much higher than that of k_3 and yet the condition R_2 ($= k_2\,[Ni\ phen_2]$) and R_1 ($= k_1\,[Ni\ phen]$) $\ll R_3$ still hold.

A value of $k_2 \sim 10k_3$ was indicated by acid-dissociation experiments [3] on $[Ni\ phen_3]^{2+}$ and $[Ni\ phen_2]^{2+}$. More recently, Margerum, Bystroff, and Banks [4] have studied spectrophotometrically the kinetics of dissociation (and formation) of $[Ni\ phen]^{2+}$ in 10^{-4}—10^{-5}-molar solutions and concentrations of hydrogen ion ranging from 0·02 to 4·5M. The results from both of these studies confirm the relation $R_2, R_1 \ll R_3$ implied in our ligand-exchange results. However, it would be interesting to determine the values of k_2 and k_1 as well as the other kinetic parameters in neutral solution in order to compare them with the values obtained for the equilibrium represented by R_3. The dissociation rate constant in neutral or weakly acid solution (which we shall see is pH-independent) refers to a process in which one phenanthroline molecule is disrupted from the complex, and the question of protonated complex species [4] probably does not arise. In addition, it will be possible to detect any direct $[Ni\ phen]^{2+}$–Ni^{2+} exchange, a type of process already encountered in several metal-exchange studies. From the measured successive stability constants for the nickel–phenanthroline system [4] it can easily be shown that with $[Ni^{2+}] \sim 5[phen]$ at pH about

* Part III, *J.*, 1957, 4456.

[1] Wilkins and Williams, *J.*, 1957, 1763.
[2] Wilkins and Williams, *J. Inorg. Nuclear Chem.*, to be published.
[3] Basolo, Hayes, and Neumann, *J. Amer. Chem. Soc.*, 1953, **75**, 5102.
[4] Margerum, Bystroff, and Banks, *ibid.*, 1956, **78**, 4211.

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6—7 $[Ni\ phen]^{2+}$ is present at least as 98% of the phenanthroline-containing species so that exchange studies can be carried out easily in these conditions with radioactive nickel tracer.

If a small amount of $^{63}Ni^{2+}$ is added to an equilibrium mixture containing comparable amounts of $[Ni\ phen_2]^{2+}$, $[Ni\ phen]^{2+}$, and Ni^{2+} then by following the specific activities of the three species against time it is possible to determine k_2 and k_1, although the accuracy of k_1 attained by this procedure is not as high as that from the exchange studies involving only two species.

TABLE 1. *Exchange of* $[Ni\ phen]^{2+}$ *with* Ni^{2+}.

Run No.	pH	Temp.	$[Ni\ phen]^{2+}$ (mmole l.$^{-1}$)	$[Ni^{2+}]$ (mmole l.$^{-1}$)	$t_{\frac{1}{2}}$ (min.)	10^5R (min.$^{-1}$ mole l.$^{-1}$)	$10^4k_{(exch)}$ (min.$^{-1}$)
1	5·5	25·0°	5·1	16·6	1120	0·24	4·72
2	6·2	45·1	5·3	16·0	61	4·52	85·2
3	6·8 [a]	45·1	5·2	16·0	62	4·38	84·3
4	5·8	45·1	2·6	8·0	67	2·03	78·1
5	5·7 [b]	45·1	4·9	14·6	37	6·87	140·2
6	—	45·1	52·0	153·0	60	44·80	86·3
7	—	45·1	26·2	179·0	72	22·00	84·0
8	—	34·9	50·4	154·0	220	11·95	23·7
9	—	34·9	21·8	210·0	301	4·54	20·8
10	1·05	25·0	45·0	145·0	310	7·65	17·0

[a] Adjusted with sodium hydroxide. [b] 0·3M-Sodium acetate–acetic acid buffer being used.

EXPERIMENTAL

Radioactive Nickel.—Nickel of high specific activity was necessary for these experiments, and this was obtained from A.E.R.E., Harwell, through the courtesy of Dr. G. B. Cook. Nickel nitrate solution [containing ^{63}Ni from irradiation of nickel metal (0·5 g.) in the Windscale pile] was purified from ^{58}Co and other possible radiochemical impurities by precipitation with dimethylglyoxime in the presence of added Fe^{3+}, Co^{2+}, Mn^{2+}, and Cr^{3+} carriers.[5] The urea is best added in small portions otherwise immediate precipitation of some of the red bulky form of nickel dimethylglyoxime (rather than the brown crystalline form) occurs. After 6 hr., nickel dimethylglyoxime was converted into nickel sulphate by heating it with concentrated sulphuric acid containing a small amount of concentrated nitric acid. This procedure was repeated until the " solution count " of the nickel solution (measured in a 20th Century Electronics solution counter) was constant. The original solution gave 40,000 counts/min.; this was reduced to a constant value of 160 counts/min. (under identical conditions) after five cycles. This solution count probably arises from very small amounts of ^{59}Ni (K-capture; E = 1·07 Mev [6]) also produced in neutron irradiation of nickel.[5] The energy of the final sample of ^{63}nickel dimethylglyoxime was measured as $E_{max.} = 0{\cdot}055 \pm 0{\cdot}003$ Mev (0·063 Mev [7]). The relation used, $E_{max.} = 1{\cdot}92R^{0{\cdot}725}$, where $E_{max.}$ is in Mev and R is the range in aluminium in g./cm.^{2} holds well for energies down to 0·15 Mev and was assumed to hold for lower energies. There was no sign of X-rays after the β-particles of ^{63}Ni had been removed by aluminium or Polythene absorbers, and less than 0·2% can be X-rays or γ-rays which are not absorbed by aluminium (9·2 mg. cm.$^{-2}$). The organic part of nickel dimethylglyoxime was not readily decomposed except by perchloric or sulphuric acid. ^{63}Nickel nitrate solution for the exchange work was therefore prepared by decomposing ^{63}nickel dimethylglyoxime with concentrated sulphuric acid. After dilution, ^{63}nickel hydroxide was precipitated and washed several times with water to remove adsorbed sulphate. The hydroxide was finally dissolved in the minimum amount of dilute nitric acid. Small amounts of this solution (0·2—0·5 ml.) were added from a Pregl micropipette to exchange solutions for each run. The molarity of this solution was estimated colorimetrically, as the red oxidised-dimethylglyoxime complex.[8]

Counting Procedure.—Counting ^{63}Ni with a mica end-window Geiger–Müller tube is an insensitive method for detecting this weak β-particle emitter, but unfortunately we did not have a 2π-flow-counter, where the sample is incorporated within the tube. All the samples

[5] Singer and Kurbatov, *J. Amer. Chem. Soc.*, 1954, **76**, 4739.
[6] Emmerich, Singer, and Kurbatov, *Phys. Rev.*, 1954, **94**, 113.
[7] " Chart of the Nuclides," General Electric Co., 1956.
[8] Vogel, " Quantitative Inorganic Analysis," Longmans, Green and Co., London, 1951, p. 654.

contained ^{63}Ni as nickel dimethylglyoxime and were prepared by slurrying acetone suspensions on large G.E.C. planchets (4·9 cm.^{2}). The value[9] of "infinite thickness" for ^{63}Ni is ~4 mg./cm.^{2}, and 12·0 ± 0·2 mg. mats of nickel dimethylglyoxime were used. Acetone was allowed to evaporate from the slurry at room temperature and a few minutes' heating at 110° completed the drying. Fine, even mats were obtained and the reproducibility by this method was about ±5%.

Exchange Runs and Separation Procedure.—(a) $[Ni\ phen_3]^{2+}$–$[Ni\ phen_2]^{2+}$ *exchange.* Tris-(phenanthroline)nickel(II) nitrate of high specific activity was prepared by the addition of excess of phenanthroline to a $^{*}Ni^{2+}$ solution of known concentration. The excess of phenanthroline was then removed by extraction with benzene, and the solution made up to known volume. A solution for exchange was prepared by mixing standard nickel nitrate solution and 1 : 10-phenanthroline in such quantities that $\bar{n}$ (the degree of formation) was approximately 2·67. With these conditions the bis- and tris-phenanthroline complexes predominate. After this solution had equilibrated at 45° for several hours a small quantity of the $[^{*}Ni\ phen_3]^{2+}$ solution was added and aliquot portions were removed for separation at various times. The separation method involved cooling in ice–water and adding sodium oxalate solution; this precipitates the purple bisphenanthroline complex. After centrifugation, the trisphenanthroline complex was precipitated as the perchlorate. Both precipitates were decomposed (nitric and perchloric acids) and converted into nickel dimethylglyoxime.

(b) $[Ni\ phen_2]^{2+}$–$[Ni\ phen]^{2+}$–Ni^{2+} *exchanges.* Nickel nitrate and phenanthroline were mixed in equimolecular amounts in water. It was known from successive stability constants for the system[4] that with such quantities an equilibrium mixture in which all three species were present in comparable amounts would result and that $[Ni\ phen_3]^{2+}$ would constitute $\leqslant$2%. Exploratory experiments discovered anionic reagents which separately precipitated the three species. Solutions containing $[Ni\ phen_2]^{2+}$ and $[Ni\ phen]^{2+}$ prepared from the solid complexes[15] were stable for several hours. Both ions gave precipitates with S^{2-}, N_3^-, CN^-, $C_2O_4^{2-}$, $PdCl_4^{2-}$, SCN^-, and $S_2O_3^{2-}$. However, $S_2O_3^{2-}$ precipitated the bisphenanthroline complex very much faster than the mono-complex; the separation therefore involved addition of $S_2O_3^{2-}$ which precipitated $[Ni\ phen_2]^{2+}$ as a yellowish-green solid. This was centrifuged and the remaining solution kept at 0° for about 5 min. to ensure complete removal of bisphenanthroline complex. During this time a little blue-green mono-compounds was occasionally precipitated; this was centrifuged off and discarded. To the resulting solution potassium thiocyanate solution was added to precipitate the mono-compound; the remainder of the procedure was as given in (c) below. Both complexes were decomposed to Ni^{2+} with nitric–perchloric acid and precipitated as nickel dimethylglyoxime. The Ni^{2+} ion remaining in solution after removal of the complexes was precipitated with dimethylglyoxime.

(c) $[Ni\ phen]^{2+}$–Ni^{2+} *exchanges.* Alcoholic dimethylglyoxime formed nickel dimethylglyoxime rapidly with $[Ni\ phen]^{2+}$ only in ammoniacal solution, and when a small amount of dimethylglyoxime was added to an equilibrated mixture of Ni^{2+} (1·0 mmole) and phenanthroline (0·20 mmole) the aquated nickel ion was preferentially attacked. This was shown by adding $^{63}Ni^{2+}$ to the above mixture and measuring the specific activity of the precipitated nickel dimethylglyoxime just after mixing and after warming for some hours had effected complete exchange. The values obtained, 531 counts/min./12 mg. and 434 counts/min./12 mg. [theory = 531 × (1·0—0·2)/1·0 = 425], respectively, confirmed that all the phenanthroline was bound and that the nickel–phenanthroline complex was unattacked by small amounts of dimethylglyoxime as long as uncomplexed nickel ion was present. Since for the conditions of this exchange the concentration of nickel ion substantially exceeds that of $[Ni\ phen]^{2+}$, following the exchange by observing the specific activities of the Ni^{2+} end was insensitive and it was difficult to detect a sharp division in the decomposition of Ni^{2+} and of $[Ni\ phen]^{2+}$ so that following the activity of the latter was not satisfactory. It was only towards the end of the study that the solid nickel monophenanthroline complex became available so that exchange experiments by adding highly active $[^{63}Ni\ phen]^{2+}$ and following the increase in Ni^{2+} ion would then have been possible. Details of a typical run are: Aqueous solutions of nickel nitrate (2—4 mmoles) and phenanthroline (0·5 mmole) were mixed, warmed for about an hour to complete formation of $[Ni\ phen]^{2+}$, made up to volume (10—200 c.c.), and allowed to settle to the desired temperature. ^{63}Nickel nitrate (0·05 mmole) was added and at various times, including very early and at completion of exchange (seven half-times), the $[Ni\ phen]^{2+}$ was precipitated as thiocyanate

[9] Schweitzer, Stein, and Nehls, *J. Phys. Chem.*, 1952, **56**, 692.

complex. This was washed and decomposed by heating it for several hours with concentrated perchloric–nitric acid. After considerable concentration the solution was diluted with water and nickel dimethylglyoxime precipitated. " AnalaR " chemicals were used and the concentration of nickel nitrate solution was determined gravimetrically. The pH was measured by a Pye " Universal " pH meter and the spectrum was determined on a Unicam S.P. 500 spectrophotometer.

Calculation of Results.—In this and all subsequent discussion, the concentrations of Ni^{2+}, $[Ni\ phen]^{2+}$, $[Ni\ phen_2]^{2+}$, and $[Ni\ phen_3]^{2+}$ will be represented by a, b, c, and d, and of the corresponding species containing ^{63}Ni by a^*, b^*, c^*, and d^*. The counting rate (in counts/min./12 mg.) of nickel dimethylglyoxime derived from each of these species will be denoted by α, β, γ, and δ, respectively, and subscripts 0 and ∞ will refer to values at zero-time and at the completion of exchange. The amount of dimethylglyoxime used represents (virtually) " infinite thickness," taking into account the window thickness (~2 mg./cm.^{2}). The count rate therefore will be proportional to the specific activity, *i.e.* $\delta \propto d^*/d$, etc., with the proportionality constant disappearing in all the equations derived.

Exchange (a). For the equilibria represented by eqn. (1)

$$R_3 = k_3 d = \frac{0{\cdot}693}{t_{\frac{1}{2}}} \cdot \frac{cd}{(c+d)} \text{ and } \therefore k_3 = \frac{0{\cdot}693}{t_{\frac{1}{2}}} \cdot \frac{\delta_0 - \delta_\infty}{\delta_0}$$

In the one run carried out in this exchange, $\delta_0 = 996$, $\delta_\infty = 656$, and $t_{\frac{1}{2}} = 27$ min., giving a value for k_3 of $87{\cdot}5 \times 10^{-4}$ min.$^{-1}$ at 45·0°.

Exchange (b). For the equilibria represented by R_1 only

$$-da^*/dt = R_1[(a^*/a) - (b^*/b)]$$

$$\therefore k_1 = \frac{R_1}{b} = \frac{1}{b}\left[-\frac{da^*}{dt}\Big/\left(\frac{a^*}{a} - \frac{b^*}{b}\right)\right] = \frac{a}{b}\left[-\frac{d\alpha}{dt}\Big/\left(\alpha - \beta\right)\right]$$

while from a consideration of that governed by R_2:

$$\frac{dc^*}{dt} = R_2\left(\frac{b^*}{b} - \frac{c^*}{c}\right) \therefore k_2 = \frac{R_2}{c} = -\frac{d\gamma}{dt}\Big/\left(\beta - \gamma\right)$$

In order to estimate a value for k_1 knowledge of the composition of the system is necessary, and a large error in the determination of k_1 can thereby be introduced; the concentration of free nickel ion in the exchange mixture can be determined by several methods and this value automatically fixes the concentration of $[Ni\ phen]^{2+}$ and $[Ni\ phen_2]^{2+}$. The spectral differences in the visible region between the species are very small,[3] so that determination of the composition based thereon is unsatisfactory. The values of α_0 and α_∞ give the ratio of free to total nickel present. Comparison of α_0 with counting rates of nickel dimethylglyoxime prepared from standard amounts of radioactive nickel and inactive nickel ion also affords an estimation of Ni^{2+} ion present in the exchange solution. Finally, the weights of nickel dimethylglyoxime obtained from each species, separated as described in the exchange procedure, give an indication of their respective amounts. There was a good deal of variation in the results obtained by these methods and mean values used were Ni^{2+}, 30; [Ni phen], 42; $[Ni\ phen_2]$, 28%. These values compare with ones obtained from mean values of the successive dissociation constants: Ni^{2+}, 28; [Ni phen], 46; $[Ni\ phen_2]$, 23; $[Ni\ phen_3]$, 3%. The former values were used for both runs at 25° and 45°.

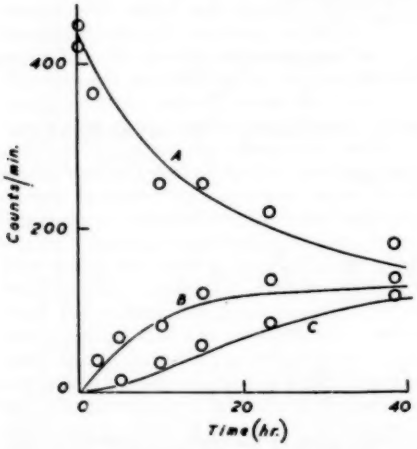
Another reason for the somewhat unsatisfactory value for k_1 is that although separation of the pure bis- and mono-phenanthroline species is possible a small amount of complexed nickel is not precipitated and continues until the Ni^{2+} stage. Finally the addition of $^{63}Ni^{2+}$ itself disturbs the chemical equilibrium slightly.

Fortunately, in order to determine k_3, which is much more valuable in view of the independent method of estimating k_1, it is necessary to know at any particular time only the rate of change of count for the bis-species (*i.e.* the tangent at that point of the curve in the Figure) and the difference in count of the mono- and bis-phenanthroline species at that time. The amounts of species undergoing exchange do not enter into the expression and the difficulties described above do not arise. From the experimental points (see Figure) three curves are

drawn, tangents are estimated for the Ni^{2+} and [Ni $phen_2$]$^{2+}$ curves at various times, and these are used to determine k_1 and k_2. The forms of the curves for [Ni phen]$^{2+}$ and [Ni $phen_2$]$^{2+}$ are such that a reasonably accurate value of k_2 is possible—the same is not as true for the determination of k_1 but even here comparison with values obtained by the accurate exchange (*c*) (below) is reasonable. By using the values of k_1 and k_2 and the composition of the exchange mixture theoretical curves may be drawn based on the relations: [9]

$$a^* = 129 + 58{\cdot}5 \exp(-0{\cdot}0023t) + 246 \exp(-0{\cdot}0094t)$$
$$c^* = 129 + 89{\cdot}0 \exp(-0{\cdot}0023t) - 218 \exp(-0{\cdot}0094t)$$

and the agreement with experimental points (especially for the mono- and bis-species) is good. The procedure was repeated at 45° so that an activation energy for the dissociation of the bis-compound could be obtained. Similarly shaped curves were obtained. The results obtained were (10^4k; min.$^{-1}$): at 25°, $k_1 = 6{\cdot}0$, $k_2 = 10{\cdot}7$; and at 45°, $k_1 = 84$, $k_2 = 126$.



The specific activities of Ni^{2+}, [Ni phen]$^{2+}$, *and* [Ni $phen_2$]$^{2+}$ *at various times in exchange* (b).

A, Ni^{2+}. *B*, [Ni phen]$^{2+}$. *C*, [Ni $phen_2$]$^{2+}$.

All fractions were radioassayed as nickel dimethylglyoxime.

During the early part (up to 5 hr.) of the tracer exchange the bis-species plays little part and this is shown by an initial induction period in the Figure. The presence of [Ni $phen_2$]$^{2+}$ being ignored, the exchange for the first 5 hr. is very similar to exchange (*c*) and by using the values for the specific activity of [Ni phen]$^{2+}$ and plotting $\log(1 - F)/t$ a straight line was obtained having $k_1 = 5{\cdot}2 \times 10^{-4}$ min.$^{-1}$, in good agreement with results of exchange (*c*) below. Allowance must be made for the fact that the specific activity at infinite time used in this calculation will be higher than that determined experimentally by an amount calculable from the concentration of bis-species present.

Exchange (c).—A simple exchange between [Ni phen]$^{2+}$ and Ni^{2+} only is being considered here, and

$$R_1 = \frac{0{\cdot}693}{t_{\frac{1}{2}}} \cdot \frac{ab}{(a+b)}$$

By varying the concentrations of the species, but always maintaining that of [Ni^{2+}] as equal to or greater than three times that of phenanthroline, so that the presence of [Ni phen]$^{2+}$ only has to be considered,[4, 10] the rate of exchange was proved to be of first order in complex concentration and independent of the concentration of nickel ion. The exchanges therefore take place completely through dissociation and an associative path involving Ni^{2+} is unimportant. No appreciable hydrolysis of Ni^{2+} occurs below pH 8.[11] The results are given in Table 1. In Run 9 [^{63}Ni phen]$(NO_3)_2$ was added to inactive nickel ion, and the decrease in activity of the [Ni phen]$^{2+}$ fraction followed. A similar result to that obtained in other runs,

[10] Sone, Krumholz, and Stammreich, *J. Amer. Chem. Soc.*, 1955, **77**, 777.
[11] Gayer and Wootner, *ibid.*, 1952, **74**, 1436.

with the different procedure indicated above, is strong evidence that the species present in all other runs, and whose exchangeability is being examined, is the mono-phenanthroline complex. Run 10 was carried out in 0·1M-nitric acid to compare with conditions used by Margerum *et al.*[4]

Preparation of [Ni phen $(H_2O)_4$]$(NO_3)_2$.—Phenanthroline hydrate (2·0 g.) and nickel nitrate hexahydrate (11·5 g.) were dissolved in warm water (25 c.c.) and the solution allowed to cool. The pale blue crystalline precipitate was washed with a small amount of ice-cold water (in which it was very soluble), and air dried [Found: C, 33·8; H, 3·7; Ni, 13·3; H_2O (Karl Fischer), 18·2. $C_{12}H_8O_6N_4Ni,4H_2O$ requires C, 33·2; H, 4·1; Ni, 13·5; H_2O, 16·5%]. The material when dried (P_2O_5) at 80° *in vacuo* lost the water (Found: Ni, 15·5; NO_3, 33·5; H_2O, 0·4. $C_{12}H_8O_6N_4Ni$ requires Ni, 16·2; NO_3, 34·1%). The solubility of this greenish-blue *compound* was similar to that of the perchlorate.[13] It did not give nickel dimethylglyoxime in aqueous alcohol but the red substance was rapidly precipitated on addition of ammonia. The substance gave a greenish precipitate with sodium hydroxide but this was not nickel hydroxide [15] since it dissolved in hot water and was reprecipitated on cooling. It appears to be the monophenanthrolinenickel(II) hydroxide. Rough magnetic measurements on the anhydrous compound indicated two unpaired electrons ($\mu \simeq 2{\cdot}7$ B.M.).

Discussion

The results of the present work, as well as data for the dissociation of [Ni $phen_3$]$^{2+}$ ion,[1] are collected in Table 2.

Table 2. *Kinetic data for the dissociation of nickel phenanthroline complexes in aqueous solution at* 25·0°.

Ion	10^4k (min.$^{-1}$)	E_{act} (kcal. mole^{-1})	$\Delta S^{\ddagger}$ (e.u.)	$\Delta S_1^{\ddagger}$ (e.u.)	log PZ (min.$^{-1}$)
[Ni $phen_3$]$^{2+}$	4·6	25·2	0·9	− 6·9	15·2
[Ni $phen_2$]$^{2+}$	10·7	23·1	−4·6	−12·5	14·0
[Ni phen]$^{2+}$	5·3	26·2	4·6	−3·2	16·0

$\Delta S^{\ddagger}$ computed from value of k given; $\Delta S_1^{\ddagger}$ obtained from value of k given by $R = k$ [complex] [H_2O], in both cases $k = (ekT/h) \exp(\Delta S^{\ddagger}/R) \exp(-E_{act}/RT)$ being used.[12]

The striking feature is the similar values for the rates of dissociation and the energies of activation of the tris- and mono-phenanthroline species. Even although the bis-species dissociates with an apparently higher rate than the other two, a factor not more than two is involved and this might be high in view of the inaccuracies inherent in the determination. Certainly the rate of removal of one phenanthroline molecule from the tris-species is no slower than from the mono-, and evidently a scheme of the kind commencing with a slow bimolecular aquation of the tris-species and ending with fast spontaneous heterolysis of succeeding complex ions does not operate here.[13] From the similar values for each kinetic parameter it appears certain that the same mechanism operates throughout the sequence of changes pictured in eqn. (1). The $\Delta S_1^{\ddagger}$ values may be of the order expected [14] if an S_N2 mechanism, involving participation of water, is operative but with the paucity of kinetic information on complex ions such a correlation is very speculative.

Margerum, Bystroff, and Banks [4] found that the values of k_{-2} and k_{-3} were very close to that of k_{-1} and could not readily be determined. However, rate-constant values were estimated as 10^2—10^3 l. mole^{-1} sec.$^{-1}$, and with this value in conjunction with an equilibrium constant for K_2 (8×10^{-9}), it can be easily shown that $k_2 \sim 5$—50×10^{-5} min.$^{-1}$, a value of the same order as that obtained in neutral conditions. The variation with pH of the rate constant for dissociation of [Ni phen]$^{2+}$ was expressed by the relation: [4]

$$k_1 = ([H^+] + 0{\cdot}015)/(8{\cdot}4 \times 10^3[H^+] + 3{\cdot}6 \times 10^3) \text{ sec.}^{-1}$$

[12] Glasstone, Laidler, and Eyring, "The Theory of Rate Processes," McGraw-Hill Book Co. Inc., New York, 1941, pp. 417, 433.
[13] (*a*) Brown, Ingold, and Nyholm, *J.*, 1953, 2674; (*b*) Brown, *Revs. Pure Appl. Chem.*, 1954, **4**, 57.
[14] See, for example, (*a*) Baxendale and George, *Trans. Faraday Soc.*, 1950, **46**, 736; (*b*) ref. 3; (*c*) Postmus and King, *J. Phys. Chem.*, 1955, **59**, 1216.
[15] Pfeiffer, Dominik, Fritzen, and Werdelmann, *Z. anorg. Chem.*, 1949, **260**, 84.

It is thus apparent that the dissociation rate will be appreciably constant in solutions more alkaline than pH 3·5. The constancy of rate constant between pH 5·7 and pH 6·8 (Table 1; Runs 2—4) agrees with this but our value ($5·3 \times 10^{-4}$ min.$^{-1}$) does not agree with that extrapolated from the formula above ($2·5 \times 10^{-4}$ min.$^{-1}$). This however is perhaps not surprising, since this relation was determined from results at fairly high acidities, and slight modification of the expression to give our value on extrapolation need not seriously disturb the experimental agreement with the acid dissociation experiments. We do not think that our use of nitrate (rather than perchlorate) would account for the increased value. An exchange at pH 1·05 was also studied (Run 10); less than 1% dissociation of the mono-phenanthroline compound occurred because the reactant concentration was much higher than in the acid-dissociation experiments, where at this pH about 10% dissociation will occur. The value obtained ($17·0 \times 10^{-4}$ min.$^{-1}$) agrees reasonably with that interpolated from the formula above ($15·6 \times 10^{-4}$ min.$^{-1}$). No effect of increased ionic strength was noticed in the exchange experiments (Runs 4, 6, and 7).

During the work the blue solid [Ni phen $(H_2O)_4$]$(NO_3)_2$ was isolated simply by mixing phenanthroline with excess of nickel nitrate in concentrated aqueous solution. The pale blue solid [Ni phen $(H_2O)_4$]$(ClO_4)_2$ has been prepared by an indirect method [15] but its existence has been questioned.[16] The complex nitrate is very soluble in water, and the visible spectra corresponded closely to that calculated from the spectra of equilibrium mixtures containing Ni_{aq}^{2+} and phenanthroline in 1 : 1 and 1 : 2 molar ratios.[3] Its ultra-violet spectra had maximum molar extinction coefficients values of $34·4 \times 10^3$ (225 mμ), $34·7 \times 10^3$ (270 mμ), and $10·7 \times 10^3$ (291·5 mμ) which compare closely with values, obtained from a mixture of 2×10^{-3}M-[Ni^{2+}] and $1·5 \times 10^{-5}$M-[phen], of $36·5 \times 10^3$ (228 mμ), $36·5 \times 10^3$ (270 mμ), and $11·0 \times 10^3$ (292 mμ).[10] As would be expected the blue aqueous solution was stable during spectrophotometry.

The results of exchange (*a*) between [Ni $phen_3$]$^{2+}$ and [Ni $phen_2$]$^{2+}$ unequivocally establish $k_3 = 87·5 \times 10^{-4}$ min.$^{-1}$ at 45·0° which compares well with $k_{(\text{ligand exch})} = 95 \times 10^{-4}$ min.$^{-1}$ at 45·1° obtained previously.[1] This agreement, in addition to the results obtained with [Ni $phen_2$]$^{2+}$ and [Ni phen]$^{2+}$, confirms that the condition $R_3 \gg R_2$, R_1 (eqn. 1) holds with the ligand-exchange experiments described previously. The results emphasise that in order to equate exchange rate constants with dissociative rate constants (even when the exchange mechanism is dissociative) it is necessary to have ancillary information regarding the dissociative behaviour of the lower complex ions which may be present even only in traces.

One of the authors (M. J. G. W.) is grateful to the Department of Scientific and Industrial Research for a maintenance grant. We are indebted to Dr. D. R. Stranks for the radiochemical assay of the purified ^{63}nickel-containing material used in this work.

THE UNIVERSITY, SHEFFIELD. [*Received, May 21st*, 1957.]

[16] Brandt, Dwyer, and Gyarfas, *Chem. Rev.*, 1954, **54**, 959.

910. *Exchange Studies of Certain Chelate Compounds of the Transitional Metals. Part V.* The Rates of Dissociation of Nickel(II) and Copper(II) Complexes of Carbon-substituted Ethylenediamines.*

By R. G. Wilkins.

The rates of dissociation in aqueous acid of nickel(II) and copper(II) complexes of substituted amines, $H_2N{\cdot}CRR'{\cdot}CR''R'''{\cdot}NH_2$, decrease as alkyl substitution increases. Although these rates are fairly fast even for complexes of 2 : 3-diamino-2 : 3-dimethylbutane (tetraMeen) (R = R′ = R″ = R‴ = Me) they are slower at pH 6·8—7·0 and have been measured from $^{63}Ni^{2+}$ and [^{14}C]-2 : 3-diamino-2 : 3-dimethylbutane exchange studies. The first-order dissociation rate constant for $[Ni\ tetraMeen_2]^{2+}$ is $2{\cdot}5 \times 10^{11} \exp(-21{,}000/RT)$ and for $[Cu\ tetraMeen_2]^{2+}$ is $1{\cdot}3 \times 10^{11} \exp(-17{,}100/RT)$, both in units of sec.$^{-1}$. This shows that the increased rate for the latter is almost entirely due to a lower activation energy. On the other hand, it appears from this and the work of others that the slower rate of dissociation of $[Ni\ tetraMeen_2]^{2+}$ than of $[Ni\ en_2]^{2+}$ residues largely in a decreased *PZ* factor. The nickel and copper complexes of 2 : 3-diamino-2 : 3-dimethylpentane (R = R′ = R″ = Me; R‴ = Et) and 3 : 4-diamino-3 : 4-dimethylhexane (R = R″ = Me; R′ = R‴ = Et) show even further decreased rates of dissociation.

Tetramethylethylenediamine (2 : 3-diamino-2 : 3-dimethylbutane) † forms a complex with nickel ion which is of interest from stereochemical, thermodynamic, and kinetic viewpoints.[1] Unlike the parent ethylenediamine, which forms the three species $[Ni\ en]^{2+}$, ‡ $[Ni\ en_2]^{2+}$, and $[Ni\ en_3]^{2+}$, the tetramethyl-compound forms only the yellow diamagnetic $[Ni\ tetraMeen_2]^{2+}$ ion in which the two chelating amines are arranged in a planar disposition about the central nickel atom. Mixtures of Ni_{aq}^{2+} and $[Ni\ tetraMeen_2]^{2+}$ do not interact spectrophotometrically, indicating, almost certainly, the absence in that mixture of any appreciable amount of $[Ni\ tetraMeen]^{2+}$, while $[Ni\ tetraMeen_2]^{2+}$ does not react even with liquid 2 : 3-diamino-2 : 3-dimethylbutane to form any higher complex. Examination of the molecular model of the bisamine species shows a high steric hindrance to reaction at the fifth and the sixth position and it is unlikely that water co-ordinates even in aqueous solution since in this the yellow colour and diamagnetism [2] persist. The yellow complex does not dissociate "immediately" when placed in excess of acid [1] and this relative "inertness" to substitution is unusual behaviour for a nickel complex with an aliphatic amine. The nickel–ethylenediamine complexes dissociate completely in aqueous acid at 0° within 30 sec.[3] and in order to measure dissociation (and formation) rates involving these complexes, it is necessary to use methanol solution at low temperatures.[4] Since the rates of dissociation of metal–amine complexes are often acid catalysed,[3] it was thought worth while to study the exchange of $^{63}Ni^{2+}$ with $[Ni\ tetraMeen_2]^{2+}$ in neutral solution. Since the monoamine compound is unstable, the study will involve only two exchange species without the attendant difficulties encountered, *e.g.*, in the exchange [5] of $[Ni\ phen_2]^{2+}$ and $[Ni\ phen]^{2+}$ with $^{63}Ni^{2+}$.

The substitution of four methyl groups having such a pronounced retardation of dissociation rate, it was decided to study the effect of increased *C*-alkyl substitution of

* Part IV, preceding paper.
† A list of the amine abbreviations used in formulæ of complexes is contained in Table 1.
‡ In this and all subsequent discussion co-ordinated water will be ignored.

[1] Basolo, Yun Ti Chen, and Murmann, *J. Amer. Chem. Soc.*, 1954, **76**, 956.
[2] Lewis and Wilkins, unpublished work.
[3] Part I, Popplewell, and Wilkins, *J.*, 1955, 4098.
[4] Bjerrum, Poulsen, and Poulsen, "Proceedings of the Symposium on Coordination Chemistry," Danish Chemical Society, 1954, p. 51.
[5] Part IV, Wilkins and Williams, preceding paper.

aliphatic diamines on the dissociation rates of their nickel and copper complexes. The discernible acid dissociation of [Cu tetraMeen$_2$]$^{2+}$ in aqueous acid at 0° caused us to study the exchange of [^{14}C]-2 : 3-diamino-2 : 3-dimethylbutane with [Cu tetraMeen$_2$]$^{2+}$ and with [Ni tetraMeen$_2$]$^{2+}$ in neutral and alkaline solution.

Experimental

Preparation of Amines and Complexes.—2 : 3-Diamino-2 : 3-dimethylbutane,[6,7] 2 : 3-diamino-2 : 3-dimethylpentane,[8] and 3 : 4-diamino-3 : 4-dimethylhexane [8] were prepared by published methods. Nickel complexes were prepared by treating nickel chloride or nitrate (1 mol.) with the amine dihydrochloride or dinitrate (2·2 mols.) in concentrated aqueous solution at neutral pH. The spectrum of bis(tetraMeen)nickel(II) nitrate in aqueous solution corresponded closely to that reported,[1] with $\varepsilon_{max.} = 63{\cdot}5$ at 4300 Å (Found: C, 34·2; H, 8·0; N, 20·1. Calc. for $C_{12}H_{32}O_6N_6Ni$: C, 34·7; H, 7·8; N, 20·2%). *Bis-(3 : 4-diamino-3 : 4-dimethylhexane)nickel(II) chloride* was quite soluble in alcohol, in contrast to the other nickel–amine complexes examined (Found: C, 45·7; H, 9·9; Cl, 16·7. $C_{16}H_{40}N_4Cl_2Ni$ requires C, 45·9; H, 9·7; Cl, 16·9%). *Bis-(2 : 3-diamino-2 : 3-dimethylpentane)nickel(II) chloride* (Found: Cl, 17·9. $C_{14}H_{36}N_4Cl_2Ni$ requires Cl, 18·2%). Attempts to prepare 3 : 4-diethyl-3 : 4-dinitrohexane from 2-bromo-2-nitrobutane and 3-nitropentane [9] in alkali solution yielded an oil which did not solidify or yield the desired amine on reduction. The only solid copper complex isolated was red *bis-(2 : 3-diamino-2 : 3-dimethylbutane)copper(II) perchlorate* (Found: C, 29·5; H, 6·5. $C_{12}H_{32}N_4O_8Cl_2Cu$ requires C, 29·1; H, 6·5%) which was precipitated during the exchange studies. When heated to 110°, the substance did not acquire the more usual blue-violet colour of bisaminecopper(II) complexes.[10]

Radioactive Nickel.—This was obtained from The Radiochemical Centre, Amersham, as an aqueous nickel nitrate solution (60 c.c.) containing nickel (3·2 g.) of total activity 250 μc. It contained 12·5 μc of ^{60}Co as radiochemical impurity. In the last stages of the investigation nickel of higher specific activity was used.[5] The purification [11] and radiochemical characterisation [5] have been described previously.

Preparation of Radioactive 2 : 3-Diamino-2 : 3-dimethylbutane.—Attempts were made to prepare [^{14}C]-2 : 3-diamino-2 : 3-dimethylbutane by irradiating pure unlabelled dioxalate [6] for 2 weeks, with 5×10^{11} neutrons/cm.^{2}/sec. flux at Harwell, having in mind the work of, *e.g.*, Schrodt and Libby.[12] The irradiation product was dissolved in warm 1N-hydrochloric acid (with some effervescence from carbonate produced), nickel chloride solution added, and the pH adjusted to about 7. The yellow solution containing the nickel complex was filtered from a slight gelatinous precipitate and the complex iodide precipitated with concentrated potassium iodide solution. The iodide was converted into the nitrate,[1] which was reconverted into iodide and the cycle repeated until the [Ni tetraMeen$_2$]I$_2$ had approximately constant activity. The activity of early samples (4000 counts per min.; end-window G.M. tube) was reduced to a steady value of about 100 per min. after eight cycles; unfortunately, such activities were too low for accurate exchange work. Direct synthesis of the labelled diamine in reasonable yields was possible from [1 : 3-^{14}C$_2$]acetoxime: [1 : 3-^{14}C$_2$]Acetone (0·1 mc; 2·2 mg.; supplied by The Radiochemical Centre, Amersham) was diluted with inactive acetone (3·5 g.) and mixed with hydroxylamine sulphate (5·0 g.) and sodium carbonate (3·2 g.) in water (40 c.c.). After about 24 hr., [1 : 3-^{14}C$_2$]acetoxime was extracted with ether, and removal of the ether left white crystals (4·0 g.; m. p. 57°).

2-Bromo-2-nitro[1 : 3-^{14}C$_2$]*propane.* This was prepared from [^{14}C]acetoxime (3·9 g.) by Iffland and Yen's method.[9] The residue (3·3 g.) from the final ligroin treatment was used in the next stage without further purification.

[2-^{14}C]2 : 3-*Dimethyl-2 : 3-dinitro*[1-^{14}C]*butane.* Crude 2-bromo-2-nitro[1 : 3-^{14}C$_2$]propane (2·3 g.) in alcohol (10 c.c.) was refluxed with 2-nitropropane (1·3 g.) in aqueous sodium hydroxide

[6] Sayre, *J. Amer. Chem. Soc.*, 1955, **77**, 6689.
[7] Bewad, *Ber.*, 1906, **39**, 1231.
[8] Seigle and Hass, *J. Org. Chem.*, 1940, **5**, 100.
[9] Iffland and Yen, *J. Amer. Chem. Soc.*, 1954, **76**, 4083.
[10] Bailar, jun., "The Chemistry of Coordination Compounds," Chapman and Hall Ltd., London, 1956, p. 66.
[11] Singer and Kurbatov, *J. Amer. Chem. Soc.*, 1954, **76**, 4738.
[12] Schrodt and Libby, *ibid.*, 1956, **78**, 1267.

(0·6 g.; 2·0 c.c.).[8] An almost white solid was finally obtained (2·0 g.; Found: C, 40·6; H, 6·9. Calc. for $C_6H_{12}O_4N_2$: C, 40·9; H, 6·9%).

2 : 3-*Diamino*[2-^{14}C]-2 : 3-*dimethyl*[1-^{14}C]*butane.* Catalytic reduction of the dinitro-compound gave only poor yields, and reduction with tin and hydrochloric acid was most effective.[13] The dinitro-compound (2·0 g.) was heated at 65° with stirring with fine-mesh tin (8·0 g.) and concentrated hydrochloric acid (25 c.c.). When all the dinitro-compound had reacted the clear solution was vigorously refluxed for about 10 min., cooled, made alkaline, and steam-distilled. One or two pellets of sodium hydroxide were added to the distillate and this was steam-distilled again. The identity of the amine solution obtained was confirmed by treatment of a small portion with a slight excess of nickel nitrate solution at a pH ~7 and spectrophotometric examination of the yellow solution; acidimetric titration gave its concentration. The total amine obtained (0·88 g.) represented an overall yield (based on diluted acetone) of 20%. Since dilution of ^{14}C with ordinary carbon occurred at a mid-stage of the synthesis it was considered not worth while to carry out a determination of the radiochemical yield. By obvious methods a small amount of nickel nitrate complex containing [^{14}C]diaminodimethylbutane was prepared as well as a sample of its dihydrochloride (Found: C, 38·2; H, 9·9; N, 15·2; Cl, 37·3. Calc. for $C_6H_{18}N_2Cl_2$: C, 38·1; H, 9·6; N, 14·8; Cl, 37·5%).

Acid Dissociation Experiments.—The rates of acid dissociation of all the copper complexes and of the nickel complexes (except those of 2 : 3-diamino-2 : 3-dimethyl-butane and -pentane and 3 : 4-diamino-3 : 4-dimethylhexane) were measured, visually, as described in Part I[3] and only semi-quantitative reliance is placed on them. The disappearance of the lilac-coloured $[CuA_2]^{2+}$ (where A = diamine in this and all subsequent discussion) was followed at 0° by using 10^{-2}M-complex and 10^{-1}M-hydrochloric acid. When a colour change was not " instantaneous," the bright blue $[CuA]^{2+}$ was observed, quite distinct from the colour of the bis-amine. At these concentrations the Cu_{aq}^{2+} ion was almost colourless.

Apart from 1 : 2-diamino-1 : 2-diphenylethane (*m*-stien) and the fully alkylated diamines (which do not form a tris-complex) all lilac $[NiA_3]^{2+}$ ions dissociated " immediately " at 0°. The resultant yellow, orange-yellow, or blue bis-species then dissociated at visible rates. Blue-green mono-$[NiA]^{2+}$ species, which finally dissociated to the very pale green Ni_{aq}^{2+} ion, was detectable only with 1 : 2-diamino-2-methylpropane (*i*-bn) and *meso*-2 : 3-diaminobutane (*m*-bn). With all other bis-nickel complexes, only a gradual lightening in colour was noticed.

TABLE 1. *Approximate dissociation rates of copper and nickel complexes of amines* (A) *of the type* $H_2N{\cdot}CRR'{\cdot}CR''R'''{\cdot}NH_2$ *at* 0°.

					CuA_2^{2+} → CuA^{2+}		CuA^{2+} → Cu^{2+}		NiA_2^{2+} → NiA^{2+}		NiA^{2+} → Ni^{2+}	
					Time	k_2	Time	k_1	Time	k_2	Time	k_1
A	R	R′	R″	R‴	(sec.) [a]	(sec.$^{-1}$)	(sec.)	(sec.$^{-1}$)	(sec.)	(sec.$^{-1}$)	(sec.)	(sec.$^{-1}$)
en	H	H	H	H	<1	⩾5	< 1	⩾5	30 [c]			
pn	Me	H	H	H	<1	⩾5	< 1	⩾5	180 [c]			
i-bn	Me	Me	H	H	<1	⩾5	~3	~1·7	~3	1·7	240	0·002
m-bn	Me	H (*meso*)	Me	H	<1	⩾5	~5	~1·0	~3	1·7	600	0·001
rac-bn ...	Me	H (racemic)	Me	H	<1	⩾5	~10	~0·5	1200 [c]			
m-stien ...	Ph	H (*meso*) [d]	Ph	H	<1	⩾5	<1	⩾5	<1			
tetraMeen	Me	Me	Me	Me	15	0·33	120	0·04	4·7 [a] 8·8 [b]	0·147 [a] 0·079 [b]		
ethyltri-Meen ...	Et	Me	Me	Me	50	0·1	270	0·02	15 [a]			
diethyldi-Meen ...	Me	Et	Me	Et	200	0·025	550	0·01	50 [a]			

[a] *I.e.*, time for reaction. [b] Values refer to $t_{\frac{1}{2}}$ in min.; k_2 in min.$^{-1}$ at 24·0°. [b] Values at 18·0°. [c] Figures refer to time of complete dissociation. [d] Measurements carried out in dioxan–water (1 : 1 by vol.).

Acid dissociation rates for the " inert " yellow nickel complexes $[NiA_2]^{2+}$ (A = 2 : 3-diamino-2 : 3-dimethylbutane or -pentane or 3 : 4-diamino-3 : 4-dimethylhexane) were determined by following the optical density at 4350 Å of a solution 0·014M in complex to which 0·14M-hydrochloric acid had been added. A plot of $\log[NiA_2^{2+}]$ against time gave a linear curve over

[13] Basolo, Murmann, and Chen, *J. Amer. Chem. Soc.*, 1953, **75**, 1478.

several half-lives, and from this, a value for k_2 was estimated. The acid dissociation rate of the tetramethyl-complex was measured at 24·0° and 18·0°, allowing an approximate estimate of the energy of activation. No increased rate of dissociation was observed when the acid concentration was raised from 0·14 to 0·45M. I am grateful to Dr. D. T. Elmore for measuring the dissociation rate at pH 5·4—5·5. The rate of consumption of acid (to maintain the constant pH) was measured automatically, and periodically small portions were withdraw for measurement of optical density at 4350 Å. Both methods gave similar values for the concentration of [Ni tetraMeen$_2$]$^{2+}$ remaining at various times. The initial changes were used since formation rates were important at this pH; the value obtained was $8{\cdot}1 \times 10^{-3}$ min.$^{-1}$ at 25°. The results of the acid dissociation experiments are recorded in Table 1, and include some previous observations.[14]

Exchange Experiments.—The results are shown in Tables 2 and 3. Ni_{aq}^{2+} was precipitated by the anion component of several buffers and even in the case of ammonium acetate buffer, there was a marked enhancement of rate (Run 4). Somewhat surprisingly there was an approximately 10% decrease in rate of dissociation when the ionic strength was increased from 0·08 to 0·50M (Runs 3, 5, 12, and 13). All experiments were therefore in media of ionic strength made up to 0·5M by addition of sodium nitrate, and the pH adjusted to 6·9 ± 0·1 by addition of acid or base as required. Detection of the effect of replacement of sodium nitrate by sodium perchlorate was prevented by precipitation of complex perchlorate. Use of [Ni tetraMeen$_2$]Cl$_2$ (rather than nitrate) had no effect on the exchange rates. With early runs (1—9) $^{63}Ni_{aq}^{2+}$ was mixed with [Ni tetraMeen$_2$]$^{2+}$ since little further nickel dilution of the original radioactive nickel was possible in view of its low specific activity and the insensitive end-window counting then available. With later runs (9—14), when sensitive gas-flow 2π-counting was possible, a suitable mixture of nickel nitrate, amine dinitrate, and sodium nitrate was adjusted to pH 6·8—7·0 with dilute sodium hydroxide solution and left for some hours. Exchange was initiated by adding either $^{63}Ni^{2+}$ or [^{63}Ni tetraMeen$_2$]$^{2+}$ obtained from the original radioactive nickel. For amine exchanges, of course, [^{14}C]ligand or [Ni [^{14}C]tetra-Meen$_2$]$^{2+}$ was added. At the pH of exchange the predominant species is the bis-complex, negligible dissociation occurring with both the Ni(II) and Cu(II) complex, as was shown by simple calculation from the known stability constants of these ions [1] and confirmed by spectral examination of two of the exchange mixtures (Runs 3 and 23). The spectra were similar to the known spectra of the bis-species, $\varepsilon_{max.} = 63{\cdot}6$ at 4320 Å (63·8 at 4340 Å [1]) for nickel and $\varepsilon_{max.} = 114$ at 5450 Å (120 at 5470 Å [15]) for copper. No appreciable hydrolysis of nickel ion occurs below pH 8.[16]

Separation, Counting, and Calculation of Results.—Separation of nickel complex as [Ni tetra-Meen$_2$]I$_2$ from either nickel ion or amine was easily effected by concentrated potassium iodide solution. In metal-exchange experiments, it was then washed, and converted into nickel dimethylglyoxime, which was washed well with water and acetone. A slurry in acetone of 10 ± 0·2 mg. of the dried material was then evaporated on a large G.E.C. planchet as described previously.[5] This conversion was necessary since the matting of the complex iodide to give a fine, uniform deposit would necessitate much more material than nickel dimethylglyoxime, which can be deposited uniformly even in as small amounts as 2—3 mg. For the ligand exchange, the complex iodide was washed with alcohol and ether, dried for a short while at 110°, and matted on small planchets.[3] Since the iodide was almost insoluble in water, the other exchanging species were recovered from the filtrate after precipitation with the concentrated iodide solution. A ligand solution (at pH ~7) was added to the filtrate when this contained Ni_{aq}^{2+} and *vice versa*. In both cases the yellow complex iodide was precipitated, and treatment identical with that described above afforded similar counting materials from both " ends " of a run. This procedure was used for only a few runs, and in these good agreement in results was obtained.

A similar technique was used for the [Cu tetraMeen$_2$]$^{2+}$–[^{14}C]ligand exchanges except that a concentrated sodium perchlorate solution was used to precipitate [Cu tetraMeen$_2$](ClO$_4$)$_2$ and this material, after being washed with water, alcohol, and ether, was used as the sample for radioassay. The effectiveness of the separation was confirmed by our obtaining small exchange values at zero times. The specific activity of both these isotopes was proportional to the count rate since " infinite " or nearly " infinite " thickness of material was used.

[14] Popplewell and Wilkins, unpublished work.
[15] Jörgensen, *Acta Chem. Scand.*, 1956, **10**, 887.
[16] Gayer and Wootner, *J. Amer. Chem. Soc.*, 1952, **74**, 1436.

An examination of exchanges involving the nickel complex in Tables 2 and 3 shows that the exchange process (Rate = R, exchange half-life = $t_{\frac{1}{2}}$; A = ligand amine, B = metal, and C = complex) is adequately expressed by the relation $R_{\text{exch.}} = k_{\text{exch.}}[\text{complex}]$, where for the metal exchanges,

$$R_{\text{metal}} = \frac{0{\cdot}693}{t_{\frac{1}{2}(\text{metal})}} \cdot \frac{[\text{C}][\text{B}]}{[\text{C}] + [\text{B}]} \quad \ldots \ldots \ldots \quad (1)$$

and for the ligand exchanges,

$$R_{\text{ligand}} = \frac{0{\cdot}693}{t_{\frac{1}{2}(\text{ligand})}} \cdot \frac{2[\text{C}][\text{A}]}{2[\text{C}] + [\text{A}]} \quad \ldots \ldots \ldots \quad (2)$$

Since $R_1 \gg R_2$ for the process pictured below, even under the conditions of ligand exchange,

$$[\text{M ligand}_2]^{2+} \underset{}{\overset{R_2}{\rightleftharpoons}} [\text{M ligand}]^{2+} + \text{ligand} \quad \ldots \ldots \quad (k_2)$$

$$[\text{M ligand}]^{2+} \underset{}{\overset{R_1}{\rightleftharpoons}} \text{M}^{2+} + \text{ligand} \quad \ldots \ldots \quad (k_1)$$

then it follows that $R_{\text{metal}} = k_2[\text{C}]$ and $R_{\text{ligand}} = 2k_2[\text{C}]$.[17]

TABLE 2. *Exchange of* Ni^{2+} *with* $[Ni\ tetraMeen_2]^{2+}$ *at* pH 6·9 ± 0·1 *and ionic strength* 0·5M.

Run No.	Temp.	[Complex] (mmole l.$^{-1}$)	[Nickel] (mmole l.$^{-1}$)	$t_{\frac{1}{2}}$ exch. (min.)	10^5R (min.$^{-1}$ mole l.$^{-1}$)	10^3k_2 (min.$^{-1}$)
3 [a]	24·9°	12·3	14·2	42	10·9	8·8
4 [b]	25·2	12·2	14·2	17	26·7	21·9
5	25·1	12·2	14·1	55	8·2	6·8
6	25·2	6·1	14·2	67	4·4	7·2
7	25·0	13·8	5·2	29	9·0	6·6
8	25·0	13·8	15·0	52	9·6	7·0
9	25·1	11·9	13·8	50	8·8	7·4
10	27·6	13·7	40·1	53	13·3	9·7
11 [c]	27·6	13·7	40·1	57	12·4	9·0
12 [a]	32·5	13·7	40·1	27	26·1	19·1
13	32·5	13·7	40·1	32	22·0	16·1
14	37·7	13·7	40·1	18	39·3	28·7

[a] No added sodium nitrate. [b] Ammonium acetate buffer at pH = 7·0. [c] Diffuse light.

TABLE 3. *Exchange of* 2 : 3-*diamino*-2 : 3-*dimethylbutane with* $[Ni\ tetraMeen_2]^{2+}$ (=Ni) *and* $[Cu\ tetraMeen_2]^{2+}$ (=Cu).

Run No.	Temp.	[Ni]	[Cu]	[amine]	$t_{\frac{1}{2}}$ exch. (min.)	10^5R (min.$^{-1}$ mole l.$^{-1}$)	10^3k_2 (min.$^{-1}$)
15	25·0°	11·9	—	3·2	8·0	24·4	10·3
16 [b]	25·0	12·3	—	3·2	10·6	18·8	7·6
17 [b]	24·9	15·0	—	29·6	40	25·8	8·6
18 [b]	25·0	7·7	—	11·3	37	12·2	7·9
19 [a]	24·9	12·4	—	10·6	~0·8	—	—
20 [b]	35·0	12·9	—	14·4	10·8	59·2	23·0
21	0·7	—	10·4	12·6	3·0	181·5	174·4
22	9·9	—	10·4	12·6	1·17	465·5	447·2
23	17·7	—	13·3	15·2	0·43	1544	1164
24 [a]	0·3	—	50·0	50·0	⩽0·01	—	—

[a] pH = 9·8, otherwise pH = 6·8. [b] Ionic strength = 0·5M.

For the copper complex exchanges, however, it is believed that only the equilibrium analogous to R_2 above is responsible for ligand exchange, and the rate of exchange $R_{\text{ligand}} = k_2[\text{C}]$, since in the acid dissociation experiments (see Table 1) the second dissociation (represented by R_1) is slower than the first and that therefore this condition obtains in neutral solution as well. The exchange of Cu^{2+} with $[Cu\ tetraMeen]^{2+}$ would resolve this point.

There is a small difference between the values of k_2 estimated from nickel and amine exchanges (mean values 7·1 ± 0·4 × 10^{-3} min.$^{-1}$ and 8·0 ± 0·5 × 10^{-3} min.$^{-1}$ at 25·0° respectively): it appears to be just outside experimental accuracy, and is too large to be explained by

[17] Wilkins and Williams, *J. Inorg. and Nuclear Chem.*, in the press.

a possible ^{62}Ni isotope effect, but Runs 16, 17, and 18 indicate that there may be a slight dependence of exchange rate on ligand concentration. The value from Run 16 ($7{\cdot}6 \times 10^{-3}$ min.$^{-1}$) is close to that from Run 6 or 9 and both results agree well with the acid dissociation value at pH 5·5 ($8{\cdot}1 \times 10^{-3}$ min.$^{-1}$). The variation of rate with temperature was similar for both ligand and metal exchange with the nickel complex.

Discussion

Kinetic data pertaining to rates of dissociation of Ni(II)– and Cu(II)–aliphatic amine complexes are summarised in Table 4, and include results for nickel– and copper–ethylenediamine complexes in acid methanol.[4] All results with $[Ni\ tetraMeen_2]^{2+}$ in acid relate to a maximum rate reached by 0·03M-acid and hardly altered in 0·5M-acid. Acid has more

Table 4. *Kinetic data for the dissociation of* Ni(II)- *and* Cu(II)-*amine complexes at* 0°.

Ion	E_{act} (kcal. mole^{-1})		log PZ (sec.$^{-1}$)		log k (sec.$^{-1}$)	
	acid	neutral	acid	neutral	acid	neutral
$[Ni\ en_2]^{2+}$	19·9 [b]	—	15·7 [b]	—	−0·2 [b]	—
$[Ni\ tetraMeen_2]^{2+}$	~17·8	21·0	~10·5	11·4	−3·8 [a]	−5·4 [a]
$[Cu\ en_2]^{2+}$	~14·0 [b]	—	—	—	⩾+0·7 [c]	⩾+0·7 [c]
$[Cu\ en]^{2+}$	17 [b]	—	14 [b]	—	+0·4 [b]	—
$[Cu\ tetraMeen_2]^{2+}$	—	17·1	—	11·1	−0·5	−2·6

[a] Extrapolated value. [b] See ref. 4. [c] See ref. 3.

effect with copper than with nickel complexes of 2 : 3-diamino-2 : 3-dimethylbutane.[4] The acid dependence suggests that monoprotonated species may be involved in the acid dissociation analogous to the observations of the $[Ni\ phen]^{2+}$ and $[Fe\ dipy_3]^{2+}$ systems.[18] In fact, the approximate expression at 22·0°:

$$-\frac{d}{dt}[NiA_2] = \frac{0{\cdot}127[H^+] + 3{\cdot}3 \times 10^{-6}}{[H^+] + 5{\cdot}95 \times 10^{-4}}[NiA_2]$$

can be deduced from rate measurements at several pH's. This is the form of pH-rate dependence in which more than one metal complex is involved in dissociation at intermediate pH values. In acid dissociation experiments and in one exchange (Run 4) acetate- (and phthalate-) containing buffers enhanced rates of reaction, but caused no marked spectral change. Rates of dissociation of the 2 : 3-diamino-2 : 3-dimethylbutane complexes of copper and nickel at pH 6·8—7·0 obey the relations $k_2 = 1{\cdot}3 \times 10^{11} \exp(-17{,}100/\boldsymbol{RT})$ and $k_2 = 2{\cdot}5 \times 10^{11} \exp(-21{,}000/\boldsymbol{RT})$ sec.$^{-1}$, respectively, so the lower rate of the latter is due almost entirely to a larger activation energy. Provided that the results in methanol can be compared with those in water,[3] the slower dissociation of $[Ni\ tetraMeen_2]^{2+}$ than of $[Ni\ en_2]^{2+}$ resides almost entirely in a decreased PZ factor.

It is apparent from Table 1 that the rate of dissociation in acid decreases as alkyl *C*-substitution increases. This is not noticed with copper until the dimethyl derivative is examined, and then only at the mono-decomposition stage but the introduction of even the first methyl group with nickel reduces the rate. The introduction of two phenyl groups on the other hand has no noticeable retardation of dissociation rates for the copper and in fact enhances the dissociation rate of the nickel complex. When four methyl groups are added even the dissociation of $[CuA_2]^{2+}$ becomes discernible, the rate decreasing on successive replacement of methyl groups by one and then two ethyl groups, so that the decomposition of $[Ni\ diethyldiMeen_2]^{2+}$ in excess of acid is remarkably slow ($t_{\frac{1}{2}}$ ~50 min. at 25°). No attempt was made to separate 3 : 4-diamino-3 : 4-dimethylhexane into the theoretically possible racemic and *meso*-form but the shape of the acid-dissociation curves suggested that probably only one species was undergoing reaction. Likewise, there was no indication of a *cis*- and a *trans*-form of the nickel complex with 2 : 3-diamino-2 : 3-dimethylpentane.

[18] See, *e.g.*, Krumholz, *J. Phys. Chem.*, 1956, **60**, 87; Margerum, Bystroff, and Banks, *J. Amer. Chem. Soc.*, 1956, **78**, 4211.

This observed decreased rate, which is particularly noticed at the point of complete alkyl substitution, probably arises from two factors. If it is assumed that the dissociation process involves in fact a bimolecular reaction with water, an increasing steric and hydrophobic effect will accompany increasing *C*-alkyl substitution and appear as a marked decrease in the activation entropy term. A knowledge of the mechanism of ring opening (*i.e.*, which of the two stages is the slower) might help in a more detailed understanding of the *modus operandi* of this effect. Certainly, the decreased rate cannot be correlated with an increased thermodynamic stability of the complex, since Basolo and his co-workers [1] have shown that *C*-substitution of ethylenediamine has only a relatively small and non-systematic effect on the stability of copper and nickel complexes.

The fast exchange of [^{14}C]ligand with [Ni tetraMeen$_2$]$^{2+}$ and with [Cu tetraMeen$_2$]$^{2+}$ (Runs 19 and 24) at pH ~10 indicates that dissociation is markedly base-catalysed although the unlikely possibility exists that a direct S_N2 process involving ligand is involved under these conditions when the concentration of free amine is much higher than at neutral pH.

The kinetic stability of the nickel and copper complexes of 2 : 3-diamino-2 : 3-dimethylbutane and higher homologues suggests that complexes of these ligands with other metals, normally forming "labile" ions, might dissociate at measurable rates. For example, preliminary observations of the Co(II)–2 : 3-diamino-2 : 3-dimethylbutane complex shows that this ion does not "immediately" dissociate in aqueous acid. In addition, because of the enhanced kinetic stability, it may be possible to resolve tetrahedral complexes of mercury(II) and zinc(II) with the diaminopentane or separate the *cis*- and the *trans*-isomer of the palladium(II) complex with the same amine.

Some of this work was carried out during the tenure of a Vacation Consultancy at the Atomic Energy Research Establishment at Harwell. The author is very grateful to the Authority for the facilities provided during this appointment, and to several members of the Chemistry Division for their help and advice.

THE UNIVERSITY, SHEFFIELD. [*Received, May 21st,* 1957.]

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911. *Molecular Polarisation and Molecular Interaction. Part VII.* The Apparent Dipole Moments of Some Di- and Tri-substituted Anilines in Benzene and Dioxan.*

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The apparent dipole moments of 2 : 4- and 3 : 5-dibromoaniline, 2 : 4- and 3 : 5-dinitroaniline, 2 : 4 : 6-trinitroaniline, and 2-methyl-4-nitroaniline in benzene and dioxan have been determined from measurements on dilute solutions in these solvents. The interaction moments (μ_{int}) and the vectorial values of the additional moments in dioxan ($\Delta\mu_{vect}$) for these and allied amines have been calculated. For the disubstituted anilines μ_{int} and $\Delta\mu_{vect}$ follow the linear relation observed for *m*- and *p*-monosubstituted anilines. The values of μ_{int} for 2 : 4 : 6-tribromoaniline and 2 : 4 : 6-trinitroaniline are such as would be expected from the values for the corresponding mono- and di-substituted anilines, indicating that there is little or no steric inhibition of the mesomeric effect of the amino-group such as is observed with mesidine and aminodurene. For all aniline derivatives containing two *ortho*-groups, however, $\Delta\mu_{vect}$ is less than would be expected from the linear relationship.

THE apparent dipole moment of a primary aromatic amine in dioxan is invariably greater than in benzene.[1-3] The difference ($\Delta\mu$) has been interpreted as arising from hydrogen

* Part VI, *J.*, 1957, 3217.

[1] Few and Smith, *J.*, 1949, 753.
[2] *Idem*, *J.*, 1949, 2663.
[3] Smith, *J.*, 1953, 109.

bonding between an amino-hydrogen atom and an oxygen atom of a dioxan molecule, and from an investigation of the system aniline–dioxan–benzene evidence has been obtained that in dilute solutions of aniline in dioxan a large proportion (~65%) of the amine molecules are hydrogen-bonded to a dioxan molecule.[4] For a number of *m*- and *p*-substituted anilines $\Delta\mu$ is greater than for aniline itself, and it is particularly large when the dipole moment in benzene exceeds appreciably the value calculated by vector summation of the group moments of the substituents. Such abnormal values of the moment in benzene solution may reasonably be assumed to arise from an " interaction moment " (μ_{int}) acting along an axis parallel to the line joining the carbon atoms carrying the amino-group and the other substituent, respectively. If it is further assumed that the increased moment in dioxan solution arises from an additional component to the moment ($\Delta\mu_{vect}$) acting along the same axis as the interaction moment, it is found that, within experimental error (±0·02 D), this is given by $\Delta\mu_{vect} = 0{\cdot}33 + 0{\cdot}255\mu_{int}$.[5]

This observation gives strong support to the view that in the complexes with dioxan an appreciable increase in molecular polarisation, and consequently in apparent dipole moment, accompanies the hydrogen bonding only when it results in an increased mesomeric effect of the amino-group. It gives a particular interest, therefore, to the study of other substituted anilines, especially those in which steric inhibition of the mesomerism is possible either for the amine itself or for its complex with dioxan. Hence, the apparent dipole moments of 2 : 4- and 3 : 5-dibromoaniline, 2 : 4- and 3 : 5-dinitroaniline, 2 : 4 : 6-trinitroaniline, and 2-methyl-4-nitroaniline in benzene and dioxan have been measured. The results are summarised in Table 1, where α, β, and γ indicate the limiting values of $d\varepsilon/dw$, dv/dw, and dn^2/dw, respectively, at zero concentration, and the other symbols have their usual significance. The dipole moment values given under μ are calculated on the assumption that $P_{E+A} = [R_D]$, and those under μ' on the assumption that $P_{E+A} = 1{\cdot}05[R_D]$. The first series of values is used in the following discussion. Whenever possible the values of $[R_D]$ used are derived from refractive-index measurements on the solutions, but in certain instances the results obtained with the highly coloured solutions appeared to be vitiated by anomalous dispersion, and hence values computed from the refractivities of related compounds together with the appropriate bond refractivities were used. These are shown in square brackets in Table 1.

TABLE 1. *Summary of polarisation data.*

Aniline deriv.	Solv.*	100α	$-10^3\beta$	$10^3\gamma$	P_{∞} (c.c.)	$[R_D]_3$ (c.c.)	μ (D)	μ' (D)	Prev. values † (D)
2 : 4-Br_2	B	325	653	204	189·9	45·8	2·65	2·63	
2 : 4-Br_2	D	476	487	327	230·4	45·8	3·00	2·98	
3 : 5-Br_2	B	419	655	204	234·4	45·8	3·04	3·02	
3 : 5-Br_2	D	620	484	327	288·8	45·9	3·44	3·42	
2 : 4-$(NO_2)_2$	B	2062	495	—	745·8	[43·6]	5·87	5·85	
2 : 4-$(NO_2)_2$	D	2926	347	525	914·2	45·8	6·53	6·51	6·48
3 : 5-$(NO_2)_2$	B	1800	504	—	654·9	[43·6]	5·47	5·45	
3 : 5-$(NO_2)_2$	D	2434	325	346	758·7	43·6	5·90	5·88	5·91
2 : 4 : 6-$(NO_2)_3$ ...	B	428	578	—	222·0	[50·1]	2·90	2·87	
2 : 4 : 6-$(NO_2)_3$ ...	D	639	403	450	273·5	51·2	3·30	3·27	3·25
2-Me: 4-(NO_2)	B	2960	389	288	881·4	42·0	6·42	6·40	
2-Me: 4-(NO_2) ...	D	4053	210	671	1046·7	47·8	7·00	6·98	

* B = benzene; D = dioxan.

† Vasiliev and Syrkin, *Acta Physicochim U.R.S.S.*, 1941, **14**, 414; *J. Phys. Chem. U.R.S.S.*, 1941, **15**, 254.

The " theoretical " moments of the compounds have been calculated from the contributory group moments. For this purpose it has been assumed that the axis of the

[4] Few and Smith, *J.*, 1949, 2781.

[5] Smith and Walshaw, *J.*, 1957, 3217.

dipole in aniline is inclined at 48½° to the N–C bond.[5] For the dibromo- and dinitroanilines the contributions to the moments arising from the two bromine atoms and the two nitro-groups have been taken as 1·47 and 3·83 D, the dipole moments of *m*-dibromobenzene and *m*-dinitrobenzene, respectively, in benzene solution. The moments of the methyl and nitro-groups in 2-methyl-4-nitroaniline have been taken as equal to the dipole moments of toluene (0·37 D) and nitrobenzene (4·01 D), respectively. By combining the theoretical moments so obtained with the observed moments in benzene solution the interaction moments for the compounds have been derived. In these calculations it has been assumed that the interaction moments in the 3 : 5-disubstituted and 2 : 4 : 6-trisubstituted anilines act along the axis of the N–C bond, whilst in the 2 : 4-disubstituted anilines they act along an axis parallel to the line joining the $C_{(1)}$ and $C_{(3)}$ carbon atoms. The results are shown in Table 2, which includes, in addition to the compounds studied in the present work, data for 2 : 4 : 6-tribromoaniline, mesidine, and aminodurene. Similarly,

TABLE 2.

	$\mu_{calc.}$ (D)	$\mu_{benz.}$ (D)	μ_{int} (D)	$\mu_{dlox.}$ (D)	$\Delta\mu$ (D)	$\Delta\mu_{rect}$ (D)
2 : 4-Dibromoaniline	2·45	2·65	0·23	3·00	0·35	0·38
3 : 5-Dibromoaniline	2·74	3·04	0·33	3·44	0·40	0·43
2 : 4 : 6-Tribromoaniline ...	1·53	1·73[2]	0·28	2·00[2]	0·27	0·33
2 : 4-Dinitroaniline	4·57	5·87	1·39	6·53	0·66	0·71
3 : 5-Dinitroaniline	4·98	5·47	0·53	5·90	0·43	0·46
2 : 4 : 6-Trinitroaniline	1·53	2·90	1·65	3·30	0·40	0·43
2-Methyl-4-nitroaniline.....	5·36	6·42	1·08	7·00	0·58	0·59
Mesidine	1·53	1·45[3]	−0·13	1·57[3]	0·12	0·19
Aminodurene	1·53	1·45[3]	−0·13	1·57[3]	0·12	0·19

by combining the values of the apparent moments in dioxan solution with the calculated values of the theoretical moments and of the interaction moments the values of $\Delta\mu_{rect}$ have been deduced, the assumption being made in all cases that $\Delta\mu_{rect}$ acts along the same axis as μ_{int}.

The results for the dibromo- and dinitro-anilines follow a similar pattern to that shown by the monosubstituted anilines, and emphasise the importance of the positions of the substituents in determining the values not only of μ_{int} but also of $\Delta\mu_{rect}$. For these compounds the results all lie within ±0·02 D of the straight line, $\Delta\mu_{rect} = 0{\cdot}33 + 0{\cdot}255\mu_{int}$, suggested by the measurements on monosubstituted anilines. The interaction moments of the dibromoanilines, like those of *m*- and *p*-bromoaniline, can be interpreted as arising because the strong inductive effects of the bromine atoms increase the mesomeric effect of the amino-group. The interaction moment of 3 : 5-dinitroaniline can be similarly explained, but the high values of both μ_{int} and $\Delta\mu_{rect}$ for 2 : 4-dinitroaniline indicate that the mesomeric effects of the amino- and nitro-groups act in conjunction, as in *p*-nitroaniline. This suggests that there is little or no steric inhibition of the mesomerism of the amino-group either in the amine itself or in its complex with dioxan. The surprising feature is that, in spite of the fact that some hydrogen bonding between the amino-group and the *ortho*-nitro-group must occur, the relative values of μ_{int} and $\Delta\mu_{rect}$ fall in line with those for compounds in which no such intramolecular hydrogen bonding is possible.

The interaction moments for both 2 : 4 : 6-tribromoaniline (0·28 D) and 2 : 4 : 6-trinitroaniline (1·65 D) are such as would be expected from the values for *p*-bromoaniline [5] (0·20 D), 2 : 4-dibromoaniline (0·23 D), *p*-nitroaniline [5] (1·08 D), and 2 : 4-dinitroaniline (1·39 D). The evidence, therefore, is against any appreciable steric inhibition of mesomerism in these compounds. The interaction moments for mesidine and aminodurene, however, are −0·13 D, indicating that here the mesomeric moment of the amino-group is less than in aniline. For all the compounds with two substituents *ortho* to the amino-group the values of $\Delta\mu_{rect}$ are lower than would be expected from the linear relationship. With mesidine and aminodurene this may be due to a much greater steric opposition

to the mesomerism in the dioxan complex than in the free amine, but in 2 : 4 : 6-trinitroaniline, and possibly also in 2 : 4 : 6-tribromoaniline, complications arise through a competition between intermolecular and intramolecular hydrogen bonding.

That *ortho*-methyl groups have only a slight effect on the mesomerism of an amino-group is illustrated by the fact that μ_{int} for 2-methyl-4-nitroaniline is identical with that for *p*-nitroaniline. Since the dioxan complex can attain the near-coplanar configuration with the dioxan molecule linked to the amino-hydrogen atom remote from the methyl group, the value of $\Delta\mu_{rect}$ is also within experimental error of the value expected from the linear relationship.

The results indicate, therefore, that, provided not more than one position *ortho* to the amino-group is occupied by a substituent, the difference between the apparent dipole moments of an amine in dioxan and benzene solutions serves as a reliable guide to the extent of the mesomeric effect of the amino-group in the free amine. When both such positions are occupied, however, the mesomeric effect in the free amine may be greater than would be inferred from the $\Delta\mu_{rect}$ value.

Experimental

Materials.—Benzene and dioxan were purified and dried as described previously.[5]

2 : 4-Dibromoaniline was prepared by bromination of *p*-bromoacetanilide by Chattaway and Clemo's method [6] and subsequent hydrolysis. Repeatedly recrystallised from aqueous alcohol it had m. p. 79·5° (lit., 78—79°).

3 : 5-Dibromoaniline was prepared by reducing 1 : 3-dibromo-5-nitrobenzene (obtained from *p*-nitroaniline by Meyer, Meyer, and Jaeger's method [7]) with iron filings and concentrated hydrochloric acid in methanol. After steam-distillation from alkaline solution and repeated recrystallisation from petroleum (b. p. 40—60°) it had m. p. 55·1° (lit., 47·5—57°).

2 : 4-Dinitroaniline was prepared from 1-chloro-2 : 4-dinitrobenzene and ammonium acetate by Wells and Allen's method [8] and recrystallised from aqueous alcohol; it had m. p. 180° (lit., 180—186°).

3 : 5-Dinitroaniline was prepared by a modification of Nicolet's method,[9] 1 : 3 : 5-trinitrobenzene (15 g.) being reduced with the solution obtained by passing hydrogen sulphide into 95% alcohol (150 c.c.) and ammonia solution (*d* 0·880; 75 c.c.) until the weight increased by 6·3 g. After recrystallisation from water it had m. p. 161° (lit., 155—162°).

Picryl chloride was prepared from picric acid and phosphorus pentachloride by Brady and Horton's method,[10] and was converted into 2 : 4 : 6-trinitroaniline by treatment with ammonia in boiling nitrobenzene [11]: after removal of ammonium chloride and recrystallisation from glacial acetic acid it had m. p. 189° (lit., 187—190°).

2-Methyl-4-nitroaniline was prepared by nitrating acet-*o*-toluidide with fuming nitric acid at −5°. The product was recrystallised from alcohol and, after hydrolysis, the 2-methyl-6-nitroaniline was removed by steam distillation from acid solution: after repeated recrystallisation from aqueous alcohol the 2-methyl-4-nitroaniline had m. p. 129° (lit., 129°).

Methods and Results.—The dielectric constants, specific volumes, and refractivities of the solutions were determined at 25° by the same methods as were used in the previous investigations. The results are recorded in Table 3. For most of the series of measurements the dielectric constants of the solutions were linear with w over the concentration range used, and hence the slope of the best straight line through these points was taken as α, but where the relationship was not linear the limiting value of $d\varepsilon/dw$ at low concentration was used. In all cases both v and n^2 were linear with w and the slopes of the best straight lines were taken as β and γ, respectively. The values of $P_{2\infty}$ and $[R_D]_2$ were calculated from these parameters in the

[6] Chattaway and Clemo, *J.*, 1916, **109**, 90.
[7] Meyer, Meyer, and Jaeger, *Ber.*, 1920, **53**, 2041.
[8] Wells and Allen, *Org. Synth.*, Coll. Vol. II, p. 221.
[9] Nicolet, *J. Amer. Chem. Soc.*, 1927, **49**, 1813.
[10] Brady and Horton, *J.*, 1925, **127**, 2233.
[11] Le Fèvre, Moir, and Turner, *J.*, 1927, 2337.

usual way and checked by comparison with the values of P_2 and $[R_D]_2$ calculated from the measurements on each individual solution.

TABLE 3. *Polarisation data.*

10^6w	$10^4\Delta\varepsilon$	$10^5\Delta v$	$10^4\Delta n$	10^6w	$10^4\Delta\varepsilon$	$10^5\Delta v$	$10^4\Delta n$
2 : 4-*Dibromoaniline in benzene.*				2 : 4-*Dibromoaniline in dioxan.*			
4388	143	286	2·5	2412	115	119	2·5
8734	287	569	4·5	4653	224	228	4·5
12,675	419	827	8	7255	351	357	8
15,007	501	978	9	9416	458	459	9·5
23,899	805	1561	13·5	13,499	662	659	13·5
30,807	1037	2012	20	25,606	1265	1248	25·5
3 : 5-*Dibromoaniline in benzene.*				3 : 5-*Dibromoaniline in dioxan.*			
4847	203	316	3	3518	223	171	3
9687	408	632	6	7223	458	349	7
15,503	659	1003	10	10,220	628	495	11
21,582	916	1420	14	14,682	918	708	14
29,390	1257	1928	19	15,138	943	733	16
36,569	1568	2394	25	19,836	1246	962	22
2 : 4-*Dinitroaniline in benzene.*				2 : 4-*Dinitroaniline in dioxan.*			
165·3	36	7	—	1472	431	49	2
415·5	83	17	—	2472	725	86	3
631·2	133	32	—	3655	1071	128	7
833·5	173	39	—	5203	1523	183	10
991·0	203	49	—	6684	1953	232	12
1283·5	265	69	—	8055	2350	279	17
3 : 5-*Dinitroaniline in benzene.*				3 : 5-*Dinitroaniline in dioxan.*			
217·4	36	11	—	1172	289	37	1·5
399·2	68	20	—	2093	510	70	2·5
718·4	127	36	—	3692	907	121	4
1137	206	57	—	4781	1167	155	5
1776	323	90	—	6852	1673	217	9
2158	391	109	—	12,689	3076	409	16
2 : 4 : 6-*Trinitroaniline in benzene.*				2 : 4 : 6-*Trinitroaniline in dioxan.*			
1214	50	70	—	2377	155	95	3
2333	103	134	—	3496	224	143	5
2763	116	161	—	4536	291	181	7
3679	158	215	—	6613	425	268	12
4770	204	274	—				
5880	256	340	—				
2-*Methyl*-4-*nitroaniline in benzene.*				2-*Methyl*-4-*nitroaniline in dioxan.*			
706	209	27	0·5	6254	2510	131	15
1479	430	54	1	11,106	4375	231	25
2011	594	79	1·5	17,718	7278	378	42
3098	917	125	2·5	22,969	9347	487	56
5323	1593	205	6	35,261	14,573	741	83
6635	2024	260	7				

Grateful thanks are tendered to the Department of Scientific and Industrial Research for a Maintenance Grant (to S. M. W.) and to Imperial Chemical Industries Limited for a grant and for the loan of a precision variable condenser.

BEDFORD COLLEGE, REGENT'S PARK, LONDON, N.W.1. [*Received, April 29th,* 1957.]

XUM

912. *The Polarography of 2 : 2-Dinitropropane.*

By John T. Stock.

The polarography of 2 : 2-dinitropropane in buffered solutions of constant ionic strength, covering the approximate pH range 1—12, and in 0·1M-sodium hydroxide, has been examined. In alkaline solutions, a well-defined single wave of constant height and of half-wave potential independent of pH is obtained. This reduction wave is attributed to the formation of nitrite and the anion of the *aci*-form of 2-nitropropane. A poorly-defined second wave obtained in acid solutions appears to be due to the reduction of nitrous acid.

Although the polarography of aliphatic mononitro-compounds has received considerable attention [1,2,3] the polarographic behaviour of aliphatic dinitro-compounds has been reported by Radin and DeVries only.[4] These workers examined 1 : 3-dinitropropane, 2 : 2-dinitropropane, 1 : 5-dinitropentane, and 2 : 2-dimethyl-1 : 3-dinitropropane, but restricted their observations to five non-aqueous supporting electrolytes containing lithium chloride. We now report the polarography of 2 : 2-dinitropropane in aqueous buffer solutions of constant ionic strength, covering the approximate pH range 1—12, and in 0·1M-sodium hydroxide (pH ~13). As is clear from Radin and DeVries's results, 2 : 2-dinitropropane gives a much smaller limiting current at a given concentration than the other compounds they examined.

Experimental

Apparatus.—Current–voltage curves were obtained with a Leeds and Northrup Type E Electrochemograph, operated without damping. Data for wave-analysis and determination of half-wave potentials were obtained by manual operation, voltage measurements being checked by a dial-type potentiometer.

The polarographic cell was a 100 ml. tall beaker closed by a rubber stopper bored for the dropping mercury electrode, junction vessel, gas inlet and exit tubes, and microburette. The 12 mm. diameter junction vessel was closed at the lower end with a fine-porosity fritted glass disc and contained 0·5M-potassium chloride to match the level of the cell contents. All potentials were corrected for iR drop and referred to a large saturated calomel electrode, which was connected to the liquid in the junction vessel by an agar-saturated potassium chloride salt bridge. Cell and reference electrode were maintained at 25° ± 0·2°. On open circuit in deoxygenated 0·1M-potassium chloride at 25° the characteristics of the dropping mercury electrodes were (*A*) $m = 1{\cdot}613$ mg. sec.$^{-1}$; $t = 3{\cdot}68$ sec.; (*B*) $m = 1{\cdot}995$ mg. sec.$^{-1}$; $t = 3{\cdot}20$ sec. Most of the work was done with electrode (*B*), numerous checks being made with electrode (*A*).

Absorptiometric measurements were made with 1 cm. cells. in a Beckman model B spectrophotometer.

Reagents.—2 : 2-Dinitropropane (Commercial Solvents Corp.), recrystallised from methanol and maintained just above the m. p. for 1 hr. under vacuum, had m. p. (uncorr.) 53·5°. The material was used as an 0·100M-stock solution in 80% aldehyde-free ethanol.

Acetoxime [5] and 2-nitro-2-nitrosopropane [6] were used as 0·1M-solutions, the former in 80% ethanol and the latter in ether.

Buffer solutions were adjusted to an ionic strength of approximately 0·5 by addition of

[1] DeVries and Ivett, *Ind. Eng. Chem. Anal.*, 1941, **13**, 339; Scott, *J. Ind. Hyg. Toxicol.*, 1943, **25**, 20; Wilson and Hutchinson, *Analyst*, 1947, **72**, 432; Miller, Arnold, and Astle, *J. Amer. Chem. Soc.*, 1948, **70**, 3971; Seagers and Elving, *J. Amer. Chem. Soc.*, 1950, **72**, 3241, 5183; 1951, **73**, 947; DeVries and Bruss, *J. Electrochem. Soc.*, 1953, **100**, 445; Miquel and Condylis, *Bull. Soc. chim. France*, 1955, 236.
[2] Petru, *Coll. Czech. Chem. Comm.*, 1947, **12**, 620.
[3] Stewart and Bonner, *Analyt. Chem.*, 1950, **22**, 793.
[4] Radin and DeVries, *ibid.*, 1952, **24**, 971.
[5] Mann and Saunders, "Practical Organic Chemistry," Longmans, Green and Co., Ltd., London, 1938, 2nd edn., p. 56.
[6] Hammick and Lister, *J.*, 1937, 489.

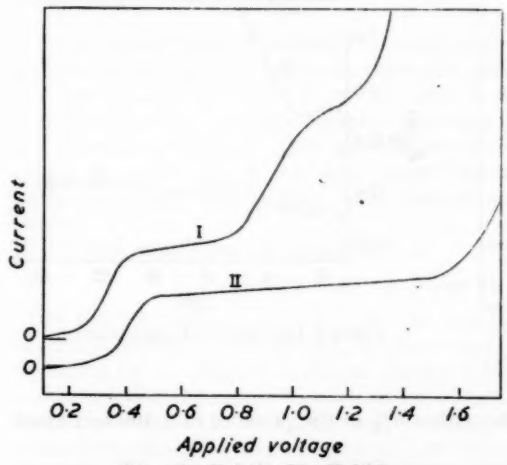
potassium chloride and checked polarographically for absence of reducible impurities. Active constituents were: up to pH 2, hydrochloric acid; [7] pH 2·2—7·8, disodium hydrogen phosphate and citric acid; [8] pH 8—10, boric acid and sodium hydroxide; pH ~11, hydrochloric acid and sodium carbonate; pH ~12, disodium hydrogen phosphate and sodium hydroxide.[7] pH values were measured by a glass electrode calibrated over the pH range 2—12.

Deoxygenation.—Oxygen was removed from a 50 ml. portion of the appropriate buffer by a stream of nitrogen, which was first bubbled through a smaller portion of the same buffer. The desired volume (<1 ml.) of the sample solution was then introduced and deoxygenation continued for a further 5 min. The change in pH caused by this procedure was negligible.

Results and Discussion

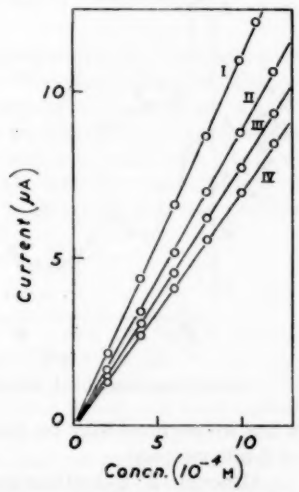
In all solutions 2 : 2-dinitropropane gave a well-defined wave without maxima and reaching full development in the region of −0·5 v (Fig. 1). In acid solution a poorly-defined second wave is also visible, but merges into the decomposition wave of the buffer

Fig. 1. *Polarograms of 2 × 10^{-4}M-2 : 2-dinitropropane with electrode A.*



Curve I, pH 2·17; II, pH 6·97.
On the vertical axis, 1 in. corresponds to 3μA.

Fig. 2. *Limiting current–concentration relations.*



Curve I, pH 1·88; II, pH 2·49; III, 3·97; IV, pH 10·18.

solution and thus exhibits no distinct region of limiting current. Since the heights of both waves increase linearly with the square-root of the pressure of mercury at the dropping electrode, they represent diffusion-controlled processes.

Measured at a fixed potential of −0·55 v, the height of the first wave in all solutions increased linearly with the concentration of 2 : 2-dinitropropane (Fig. 2). In acid conditions, however, the height of this wave for a given nitropropane concentration and given capillary characteristics depends markedly on the pH of the solution (curve I, Fig. 3). In alkaline buffers, the wave height becomes virtually independent of pH. Routine determination of 2 : 2-dinitropropane by measurement of the height of the first wave is thus best carried out in alkaline solution. Concentrations in the approximate range 10^{-5}—10^{-3}M are then directly measurable. At a given pH, borate buffers give wave heights a few per cent. greater, and half-wave potentials a few millivolts more negative, than those obtained in phosphate or carbonate buffers.

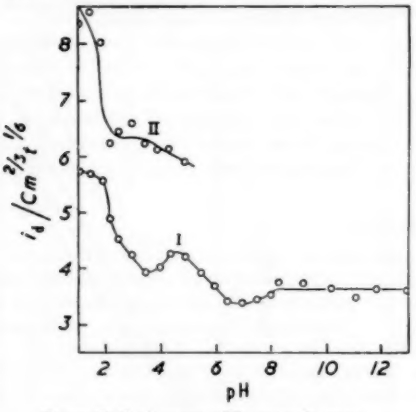
[7] Britton, "Hydrogen Ions," D. van Nostrand Co., New York, 1932, Ch. XII.
[8] Elving, Markowitz, and Rosenthal, *Analyt. Chem.*, 1956, **28**, 1179.

Although accurate measurement is not possible, the height of the second wave for a given concentration appears to be approximately constant, except in strongly acid conditions (curve II, Fig. 3). In the approximate range pH 2—3, the total height of both waves increases linearly with the concentration of 2 : 2-dinitropropane, provided that measurement is made at an appropriately-chosen potential (*e.g.*, −1·15 v at pH 2·2).

Although almost constant in alkaline buffers, the half-wave potential ($E_{\frac{1}{2}}$) of the first wave is somewhat pH-dependent in acid solution (curve I, Fig. 4), but the relation is non-linear. The half-wave potential of the second wave is very sensitive to pH (curve II, Fig. 4).

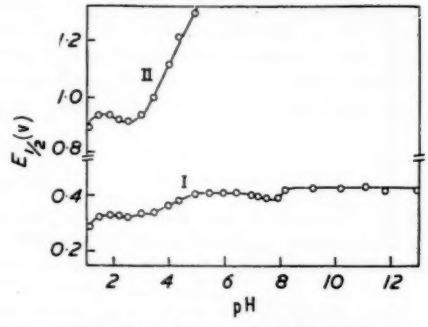
The waves of mononitroparaffins appear at potentials more negative than that required for the full development of the first wave of 2 : 2-dinitropropane. It is thus possible to determine 2 : 2-dinitropropane in the presence of much larger concentrations of mononitroparaffins, as well as in the presence of non-reducible inorganic salts, etc. For example,

FIG. 3. *Diffusion current constant–*pH *relations.*



Curve I, first wave; II, second wave.

FIG. 4. *Half-wave potential–*pH *relations.*



Curve I, first wave; II, second wave.

a few micrograms may be determined to within 5% in the presence of a 100-fold excess of 2-nitropropane.

Although 2 : 2-dinitropropane is polarographically reduced more readily than the lower aliphatic mononitro-compounds, the reduction stage corresponding to the first wave is less complete than that of a mononitro-compound. Thus, at pH 7, the wave height of 2 : 2-dinitropropane is approximately half that of a fresh solution of 2-nitropropane of similar concentration. Since Petru [2] has shown that the principal wave of nitroparaffins involves 4 electrons, the polarographic reduction of 2 : 2-dinitropropane in neutral or alkaline media presumably involves the uptake of 2 electrons. This conclusion is borne out by application of the Ilkovič equation $i_d = 607nD^{\frac{1}{2}}Cm^{2/3}t^{1/6}$ where the terms have their usual significance.[9] Assuming that the 2 : 2-dinitropropane molecule and the 2-nitropropionate ion have the same diffusion coefficient D, we can estimate the latter from the relation $D = 2{\cdot}67 \times 10^{-7}\ \lambda^\circ/z$, where λ° is the equivalent conductance of the ion at infinite dilution and z is its charge.[10] For the 2-nitropropionate ion, λ° is 32 ohm^{-1} equiv.$^{-1}$,[11] giving $D = 0{\cdot}85 \times 10^{-5}$ cm.^{2} sec.$^{-1}$ at 25°. This leads to $n = 2{\cdot}02 \pm 0{\cdot}08$ for the approximately constant wave height in alkaline solutions.

[9] Kolthoff and Lingane, "Polarography," Interscience Publishers, Inc., New York, 2nd edn., Vol. I, p. 63.

[10] *Idem, op. cit.*, p. 52.

[11] "International Critical Tables," McGraw-Hill Book Co., Inc., New York, 1929, Vol. VI, pp. 259 and 264.

That the reduction of 2 : 2-dinitropropane in alkaline solution involves the uptake of two electrons per molecule was confirmed by coulometric electrolysis [12] in 50 ml. of previously-deoxygenated 0·1M-sodium hydroxide. The stirred mercury-pool cathode was maintained at $-0{\cdot}85 \pm 0{\cdot}03$ v and a coulometer similar to that of Lingane and Small [13] was used. Results are summarised in Table 1.

Since the half-wave potential in the alkaline region is almost independent of pH, it

TABLE 1. *Reduction of 2 : 2-dinitropropane in 0·1M-sodium hydroxide.*

2 : 2-Dinitropropane taken (mmoles) ...	0·05	0·10	0·15	0·20	0·25
Coulombs reqd. Found and (calc.) ...	10·0 (9·7)	19·4 (19·3)	29·7 (29·0)	38·9 (38·6)	48·2 (48·3)
Nitrite found (mmoles)	0·05	0·09	0·16	0·20	0·24
Relative " acetone " reaction	0·5	1·0 *	1·2	2·2	2·5

* Arbitrarily assigned unit intensity.

is unlikely that hydrogen ions are directly involved in the electrode process. It is possible that the reduction product is 2-nitro-2-nitrosopropane, formed according to

$$Me_2C(NO_2)_2 + H_2O + 2e^- \longrightarrow Me_2C(NO)NO_2 + 2OH^- \quad . . . . . (1)$$

Pearson and Evans [14] inferred that such substances are formed during the electrolysis of nitroparaffins between platinum electrodes, and Bahner [15] has shown that, in alkaline solution, 2-nitropropane gives rise to some 2 : 2-dinitropropane at a platinum anode. In a pH 12 buffer, the polarographic reduction of 2-nitro-2-nitrosopropane commenced at a potential of approximately zero and the wave height decreased with time. In acid buffers the much more stable wave height increased linearly with the concentration of 2-nitro-2-nitrosopropane. This easily-reduced compound is therefore not the product sought.

Another stoicheiometric possibility is

$$Me_2C(NO_2)_2 + 2e^- \longrightarrow Me_2C{:}NO^- + NO_2^- \quad . . . . . (2)$$

In this connection, acetoxime gave no reduction wave in any of the buffers and, in alkaline solutions of sodium salts, nitrate is not polarographically reducible.[16] Further, acetoxime (or its anion) is stable in alkaline solution. However, aliquot portions of the coulometric solutions gave no reaction for nitrate [17a] but yielded strong and reproducible positive results in the 1-naphthylamine–sulphanilic acid test for nitrite.[17b] Determined absorptiometrically by this test, the yield of nitrite was one mole per mole of 2 : 2-dinitropropane taken [Table 1, rows (i) and (iii)]. Blanks containing unreduced 2 : 2-dinitropropane or acetoxime gave negligible results. Presumably the electrode reaction is of the form:

$$Me_2C(NO_2)_2 + 2e^- \longrightarrow [Me_2C{\cdot}NO_2]^- + NO_2^- \quad . . . . . (3)$$

After acidification with hydrochloric acid, portions of the coulometric solutions containing the reduction products gave no immediate reaction with 2 : 4-dinitrophenylhydrazine; a slight turbidity on standing suggested the formation of a carbonyl compound. Aliquot parts of the coulometric solutions were therefore diluted to 5 ml. with water, and 5 ml. of 50% v/v sulphuric acid were added to each. Each mixture was gently heated for 5 min., then 3 ml. were distilled off and collected at a rate of 0·2 to 0·3 ml. per min. The distillates all gave a positive acetone reaction with alkaline salicylaldehyde.[18,19]

[12] Lingane, " Electroanalytical Chemistry," Interscience Publishers, Inc. New York, 1953, p. 368.
[13] *Idem, op. cit.*, p. 353.
[14] Pearson and Evans, *Trans. Amer. Electrochem. Soc.*, 1943, **84**, 173.
[15] Bahner, *Ind. Eng. Chem.*, 1952, **44**, 317.
[16] Kolthoff and Lingane, *op. cit.*, p. 533.
[17] " Standard Methods for the Examination of Water, Sewage, and Industrial Wastes," American Public Health Association, Inc., New York, 1955, (*a*) p. 149; (*b*) p. 153.
[18] Csonka, *J. Biol. Chem.*, 1916, **26**, 209.
[19] Thomson, *J. Soc. Chem. Ind.*, 1946, **65**, 121.

Absorptiometric comparison showed that the intensity of the reaction was approximately proportional to the amount of 2 : 2-dinitropropane initially present [Table 1, rows (i) and (iv)]. Other aliquot parts similarly distilled formed immediate precipitates with 2 : 4-dinitrophenylhydrazine. Paper chromatography [20,21] showed that the precipitates were mixtures of the 2 : 4-dinitrophenylhydrazones of acetone and acetaldehyde. The acetone derivative was separately eluted and confirmed by mixed m. p.

The production of acetone suggests that the anion $[Me_2C{:}NO_2]^-$ is that of the *aci*-form of 2-nitropropane.[22] Support for this conclusion was obtained by dissolving 2-nitropropane in 0·1M-sodium hydroxide, then distilling portions of the solution with sulphuric acid. The distillates behaved similarly to those obtained from the coulometric solutions. Petru [2] has shown that, in alkaline buffers, the wave heights of nitroparaffins diminish with time, and attributes this to the conversion of the molecular form into the anion of the *aci*-form, which is not polarographically reducible.

In acid solutions, the minimum at about pH 4 in the wave height–pH curve (Fig. 3, curve I) suggests that competing reductions may be involved. However, the half-wave potential–pH curve (Fig. 4, curve I) does not support this. Further, a linear plot of $\log i/(i_d - i)$ against potential [23] was obtained for all the solutions examined, the slope being almost independent of pH (Table 2). Since the polarographic reduction of 2 : 2-dinitropropane, like that of other nitro-compounds,[2] is probably irreversible, no significance is attached to the magnitude of the slope. Reduction of the un-ionised *aci*-form $Me_2C{:}NO_2H$ or catalytic discharge of hydrogen ions may account for the increased wave height in acid solutions. Since the half-wave potential of 2-nitropropane is given by $-E_{\frac{1}{2}} = 0{\cdot}658 + 0{\cdot}037\text{pH}$,[3] the increased wave height cannot be attributed to reduction of this substance formed by rearrangement of the *aci*-form.

TABLE 2. *Analysis of first wave of* 2 : 2-*dinitropropane* ($c = 2 \times 10^{-4}$M).

pH	1·48	3·44	5·44	6·40	11·80
Reciprocal of slope	0·065	0·062	0·066	0·068	0·069

In the region pH 2·5—5, the height of the second wave is about that required for a 3-electron reduction and the half-wave potential of about −1·0 v changes by approximately 0·20 v per pH unit. This suggests that the second wave is due to the reduction of nitrous acid, for which Keilin and Otvos [24] give

$$HNO_2 + 3H^+ + 3e^- \longrightarrow \tfrac{1}{2}N_2 + 2H_2O \quad \ldots\ldots\ldots \quad (4)$$

According to them, the wave occurs at about −1·0 v. The increased height in strongly acid solution may be due to the superimposition upon the nitrous acid wave of waves due either to the reduction of the *aci*- or the nitro-form of 2-nitropropane or intermediate reduction products, or to the catalytic discharge of hydrogen ions.

The author thanks Dr. M. E. Morgan for the chromatographic separation and identification of the 2 : 4-dinitrophenylhydrazones, and acknowledges support by the U.S. Navy Department. Bureau of Ordnance. The 2 : 2-dinitropropane was a gift from the Commercial Solvents Corporation.

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STORRS, CONNECTICUT, U.S.A. [*Received, May 10th*, 1957.]

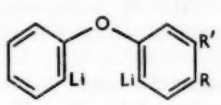
[20] Jackson and Morgan, *J. Dairy Science*, 1954, **37**, 1316.
[21] Morgan and Anderson *ibid.*, 1956, **39**, 253.
[22] Johnson and Degering, *J. Org. Chem.*, 1943, **8**, 10.
[23] Kolthoff and Lingane, *op. cit.*, p. 193.
[24] Keilin and Otvos, *J. Amer. Chem. Soc.*, 1946, **68**, 2665.

913. *The Preparation and Properties of* 10 : 10-*Disubstituted Phenoxsilanes.*

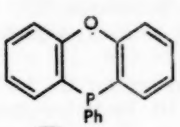
By Christopher H. S. Hitchcock, Frederick G. Mann, and A. Vanterpool.

The preparation, properties, and stereochemistry of certain 10 : 10-disubstituted phenoxsilanes and of *spiro*bis-10-phenoxsilane are discussed. Although this spirocyclic compound is readily prepared and stable, attempts to synthesise methyl-substituted derivatives failed, the products being stable silanols in which the hydroxyl group undergoes strong intramolecular hydrogen bonding.

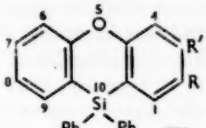
It has been shown by Mann and Millar [1] that 2 : 2′-dilithiodiphenyl ether (I; R = R′ = H), prepared by the action of *n*-butyl-lithium on the 2 : 2′-dibromo-ether, reacts with dichlorophenylphosphine, $PhPCl_2$, to form 10-phenylphenoxphosphine (II) in 63% yield. This reaction, showing the marked predominance of cyclisation over linear condensation, indicated that other reagents having two reactive chlorine atoms might also give the corresponding cyclic derivatives in good yield.



(I)



(II)



(III)

This we find to be the case. Dichlorodiphenylsilane, Ph_2SiCl_2, reacts with the dilithio-derivative (I; R = R′ = H) to form 10 : 10-diphenylphenoxsilane (III; R = R′ = H) in 59% yield, and the 10 : 10-dimethyl analogue is similarly formed in 78% yield. Moreover, the dilithio-derivative reacts very readily with silicon tetrachloride to form *spiro*bis-10-phenoxsilane (IV).

These results were obtained in 1953—1954.[2] It has recently been shown by Oita and Gilman [3] that *n*-butyl-lithium reacts directly with diphenyl ether to give the dilithio-derivative (I; R = R′ = H), from which the diphenyl derivative (III; R = R′ = H), its dimethyl analogue, and the spirocyclic derivative (IV) have similarly been prepared.

The stereochemistry of the diphenylphenoxsilane (III; R = R′ = H) and the spirocyclic derivative (IV) is of considerable interest. A tricyclic system consisting of two *o*-phenylene rings linked through two central atoms, such as the oxygen and silicon atoms in the compound (III), will be planar only if the intervalency angles subtended within the central ring by these atoms closely approach 120°.[4] If these angles are appreciably less than 120°, as in the phenoxarsines [5] and 5 : 10-dihydroarsanthrens,[6] the molecule will necessarily be folded about an axis through these central atoms.

No precise information is available regarding the intervalency angles at the silicon and oxygen atoms within the ring in the phenoxsilane system. The C–O–C angle can adjust itself to structural requirements over a wide range: for example, it is 61·6° in ethylene oxide,[7] 108° ± 3° in diethyl ether,[8] 112° ± 5° in 1 : 4-dioxan,[8,9] 124° ± 5° in diphenyl

[1] Mann and Millar, *J.*, 1953, 3746.
[2] Vanterpool, Ph.D. Diss., Cambridge, 1954; *Abs. Cambridge Diss.*, 1953—1954, p. 246 (Cambridge Univ. Press, 1956).
[3] Oita and Gilman, *J. Amer. Chem. Soc.*, 1957, **79**, 339.
[4] Campbell, Le Fèvre, Le Fèvre, and Turner, *J.*, 1938, 404.
[5] Lesslie and Turner, *J.*, 1934, 1170.
[6] Chatt and Mann, *J.*, 1940, 1184.
[7] Cunningham, Boyd, Myers, Gwinn, and Le Van, *J. Chem. Phys.*, 1951, **19**, 676.
[8] Cf. Allen and Sutton, *Acta Cryst.*, 1950, **3**, 46.
[9] Hassel and Viervoll, *Acta Chem. Scand.*, 1947, **1**, 149, give 108° ± 5°.

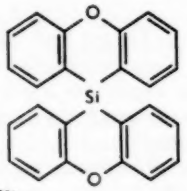
ether,[10] and 123° ± 1° in di-*p*-bromodiphenyl ether [11] and its iodo-analogue.[12] In spite of these values for free diphenyl ethers, the C–O–C angle in the phenoxsilane ring system might be less than 120°, particularly if there is a strong tendency for the C–Si–C angle to attain 109°; consequently the molecule might be folded about the O–Si axis.

Apart from *X*-ray crystal analysis, evidence for this folding could be sought in two directions, chemical and physical. First, a derivative of the phenoxsilane (III) having a substituent in one of the *o*-phenylene rings should be resolvable into optically active forms if the ring system is stably folded. We have, therefore, prepared 2-methyl-10 : 10-diphenylphenoxsilane (III; R = Me, R′ = H) (55% yield) by interaction of 2 : 2′-dilithio-4-methyldiphenyl ether (I; R = Me, R′ = H) and dichlorodiphenylsilane, and converted it with *N*-bromosuccinimide into the 2-bromomethyl derivative (III; R = CH_2Br, R′ = H). Attempts to convert the bromomethyl group into an acidic or basic group for optical resolution proved, however, unsatisfactory. The bromomethyl compound (III; R = CH_2Br, R′ = H) gave no decisive product when brought into reaction with ethyl sodiomalonate or potassium cyanide, or hexamethylenetetramine with subsequent hydrolysis of the crude hexaminium salt.[13] and it failed to react with ammonia under various conditions or with potassium phthalimide. The 2-dibromomethyl derivative (III; R = $CHBr_2$, R′ = H) resisted normal hydrolysis, but with silver nitrate in aqueous 2-ethoxyethanol solution, gave the 2-aldehyde (III; R = CHO, R′ = H), which did not crystallise and was identified solely as its 2 : 4-dinitrophenylhydrazone. Work on these lines was therefore abandoned.

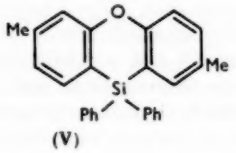
Secondly, it appeared that evidence for the folded structure might be obtained by comparing the dipole moments of 10 : 10-diphenylphenoxsilane (III; R = R′ = H) and its 2 : 7-dimethyl derivative (V). Mr. E. W. Randall and Dr. L. E. Sutton, who have kindly investigated our compounds, find that these two derivatives in benzene solution have dipole moments of 0·97 ± 0·03 and 1·01 ± 0·03 D respectively. They report:

" It is not possible to form any definite conclusions regarding the angle between the aromatic ring planes because (i) the total moments are small, and the precision of the measurements is, therefore, relatively poor; moreover, error due to neglect of atom polarisation may be considerable; (ii) the substitution moments due to the methyl groups are small, so the change in total moment is insensitive to change in interplanar angle.

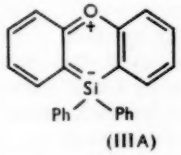
" If, however, the total moments are taken at their face value and reasonable assumptions (see below) are made concerning bond lengths and bond moments, the interplanar angle is calculated as 165—158° for (III; R = R′ = H) and as 158—154° for (V).



(IV)



(V)



(IIIA)

These angles would be considerably larger if the $_AP$ terms were appreciable. The effect of contributions from structures such as (IIIA) upon the calculations would be to make the angles smaller, although on physical grounds one expects such contributions to make the tricyclic system planar.

" The assumptions made are: (i) That the O–C bond moment is 1·16 D. This is

[10] Coop and Sutton, *J.*, 1938, 1869.
[11] Toussaint, *Mem. Soc. roy. Sci. Liège*, 1952, **12**, 1.
[12] Toussaint, *Bull. Soc. Sci. Liège*, 1946, **15**, 86.
[13] Cf. Angyal, Morris, Tetaz, and Wilson, *J.*, 1950, 2141; Wood, Tung, Perry, and Gibson, *J. Amer. Chem. Soc.*, 1950, **72**, 2992.

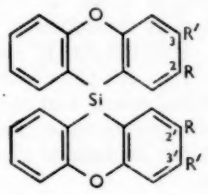
derived from the value, 1·16 D, for the moment of diphenyl ether [14] and an assumed C–O–C angle of 120°; [10,15] (ii) that the methyl substitution moment is 0·40 D; [16] (iii) that the contributions of the Si–C bond moments can be ignored because of the approximate symmetry of the bonds around the silicon and the probable small magnitude of the moment; [17] (iv) that the bond lengths are 1·84 Å for Si–C, 1·40 Å for C–C, and 1·40 Å for C–O.[18]

" A simple stereochemical calculation based on the above bond lengths, and values of 120° and 109° respectively for the oxygen and silicon bond angles, shows that the model with the least angular strain has an interplanar angle of 150°.

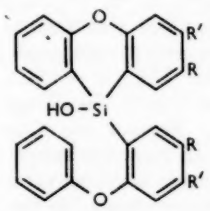
" From these two sets of calculations it would appear that the interplanar angle is between 150° and 160°."

It is clear, therefore, that dipole studies of this type require phenoxsilanes containing substituents, such as chlorine, which are more polar than methyl groups, but the synthesis of these chloro-derivatives presents considerable difficulties.

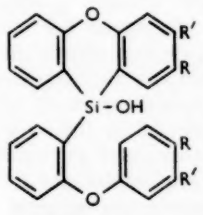
The investigation of the stereochemistry of the spirocyclic system in *spiro*bis-10-phenoxsilane (IV) has revealed an unexpected factor. If each phenoxsilane unit in this compound is folded about the O–Si axis, and the silicon atom has the usual tetrahedral angle, the compound is dissymmetric and should be capable (if the folding is stable) of existing in optically active forms. If a substituent group is inserted in two corresponding positions in the molecule, giving for example the 2 : 2′-dimethyl derivative (VI; R = Me, R′ = H) or the 3 : 3′-dimethyl derivative (VI; R = H; R′ = Me), these products should each exist in two racemic forms.



(VI)



(VII)



(VIII)

We have attempted to prepare such substituted compounds both by direct substitution in the compound (IV), and by synthesis, whereby the positions of the substituents would be clearly defined.

The compound (IV) possesses considerable stability. This is shown by the fact that 2 : 2′-dilithiodiphenyl ether (I; R = R′ = H), when treated even with one molecular equivalent of silicon tetrachloride, forms the spirocyclic derivative (IV), apparently to the exclusion of 10 : 10-dichlorophenoxsilane. Further, we have recovered the spiro-compound (IV) unchanged after it had been treated with fuming nitric acid in hot acetic anhydride solution, with bromine in boiling chloroform solution, and with *N*-bromo-succinimide and benzoyl peroxide in boiling carbon tetrachloride solution. The use of more vigorous conditions appeared to cause extensive rupture of the cyclic system, and no decisive products could be isolated. This high stability of the compound (IV) makes the direct preparation of substituted derivatives apparently impracticable.

In view of the ready formation of 2-methyl-10 : 10-diphenylphenoxsilane (III; R = Me, R′ = H) in 55% yield of purified material by the interaction of dichlorodiphenylsilane and

[14] Hampson, Farmer, and Sutton, *Proc. Roy. Soc.*, 1933, *A*, **143**, 147.
[15] Maxwell, Hendricks, and Mosley, *J. Chem. Phys.*, 1935, **3**, 699.
[16] Everard and Sutton, *J.*, 1951, 2807.
[17] Freiser, Eagle, and Speier, *J. Amer. Chem. Soc.*, 1953, **75**, 2821.
[18] " Table of Interatomic Distances and Molecular Configurations," forthcoming Special Publication of the Chemical Society.

2 : 2′-dilithio-4-methyldiphenyl ether (I; R = Me, R′ = H), we treated the latter with silicon tetrachloride in order to obtain 2 : 2′-dimethyl*spiro*bis-10-phenoxsilane (VI; R = Me, R′ = H). Thorough purification of the crude product yielded, however, solely (17% yield) 10-hydroxy-2-methyl-10-(5-methyl-2-phenoxyphenyl)phenoxsilane (VII; R = Me, R′ = H) or its 10-*o*-(*p*-tolyloxy)phenyl isomer (VIII; R = Me, R′ = H). Consequently the desired spirocyclic system had apparently not been formed, in marked contrast to the ready formation of the unsubstituted spiran (IV).

We find similarly that, although 2 : 2′-dilithio-5-methyldiphenyl ether (I; R = H, R′ = Me) reacts with dichlorodiphenylsilane to give 3-methyl-10 : 10-diphenylphenoxsilane (III; R = H, R′ = Me) in 43% yield, it reacts with silicon tetrachloride to give a crude product from which the silanol (VII; R = H, R′ = Me) or its isomer (VIII; R = H, R′ = Me) has been isolated in low yield.

The presence of a methyl group in 2 : 2′-dilithiodiphenyl ether appears, therefore, to inhibit the formation of the spirocyclic system, while not affecting that of the initial phenoxsilane ring system. Other examples are known of the influence of nuclear methyl substituents on heterocyclic-ring formation in entirely different systems, such as Mole and Turner's quantitative study of the effect of such groups on the cyclisation of 2-dichloroarsinodiphenyl ether derivatives to the corresponding phenoxarsines,[19] but complete inhibition of ring formation by a nuclear methyl group which is not exerting steric obstruction is rare.

We have investigated in some detail the properties of the silanol (VII or VIII; R = Me, R′ = H), which is the more readily obtained. This silanol also has considerable stability. When first isolated, it was thought to be the spiran (VI; R = Me, R′ = H) and that the persistent low carbon content was due to analytical difficulties. It was, therefore, converted into the bromomethyl compound (VII; R = CH_2Br, R′ = H) and thence into the aldehyde compound (VII; R = CHO, R′ = H). All three compounds gave analytical results in accordance with the silanol structure, which had apparently been unaffected by these reactions. Further, the silanol sublimes with some charring at 380°/760 mm., and the sublimate on recrystallisation yields the unchanged silanol: in contrast, triphenylsilanol at 280° yields hexaphenyldisiloxane.

In experiments designed to give evidence for the hydroxyl group, the silanol was recovered after treatment with thionyl chloride, with ethanolic zinc chloride, and with *n*-butyl-lithium followed (in separate experiments) by methyl iodide, benzoyl chloride, and toluene-*p*-sulphonyl chloride.

To determine whether the two silanols were of type (VII) or (VIII), their infrared spectra have been studied. These spectra appeared to show decisively that both silanols are of the type (VIII), for neither shows a band at 13·5 μ characteristic of a monosubstituted benzene ring, but both show a strong band at 13·2 μ characteristic of an *o*-phenylene group, and in this respect resemble the spiran (IV). These results are in marked contrast to those of 10 : 10-diphenylphenoxsilane and its 2- and 3-methyl derivatives, which do show both these bands (cf. Table).

Benzene substitution bands in Nujol mull.

	13·2 μ region	13·5 μ region
Silanol (VII–VIII; R = Me, R′ = H)	13·25	—
Silanol (VII–VIII; R = H, R′ = Me)	13·2	—
10 : 10-Diphenylphenoxsilane (III; R = R′ = H)	13·15	13·5
2-Methyl-10 : 10-diphenylphenoxsilane (III; R = Me, R′ = H)	13·2	13·5
3-Methyl-10 : 10-diphenylphenoxsilane (III; R = H, R′ = Me)	13·1	13·55
Spiran (IV)	13·2	—

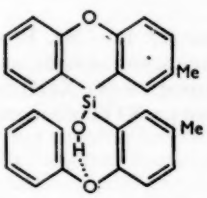
This apparently sharp differentiation of the two classes may, however, be false, for phenol and anisole show bands corresponding to the phenyl group at 753 cm.$^{-1}$ (13·30 μ)

[19] Mole and Turner, *J.*, 1939, 1720.

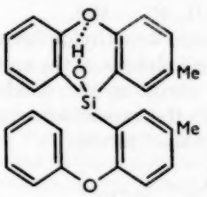
and at 756 cm.$^{-1}$ (13·25 μ) respectively,[20] and diphenyl ether at 748 cm.$^{-1}$ (13·4 μ). This shift of the phenyl band to lower μ values when this group is attached to oxygen means that the silanols might be of type (VII) and that the phenyl band now coincides with the *o*-phenylene band. Hence this structural point remains undecided. For convenience, these silanols will be referred to subsequently as type (VII).

The infrared spectra of the silanols showed, moreover, no indication of a hydroxyl group. Now the silicon atom in silanols has no influence on the O–H stretching vibrations, except when hydrogen bonding occurs. Consequently free ≥Si·OH groups usually absorb strongly in the normal region, 3690—3590 cm.$^{-1}$. Intermolecular hydrogen bonding normally shifts this sharp band to a lower frequency, with increase in the intensity of the band. This type of hydrogen bonding is usually destroyed on dissolution of the silanol, and the normal sharp band appears. Thus triphenylsilanol in carbon tetrachloride solution shows a strong band at 3690 cm.$^{-1}$, but in Nujol mull shows a broad band at 3250 cm.$^{-1}$, indicating intermolecular hydrogen bonding in the solid state.[21]

The two silanols (VII; R = Me, R′ = H) and (VII; R = H, R′ = Me) in either Nujol mulls or carbon tetrachloride solution showed no bands between 2500 and 3700 cm.$^{-1}$, except the sharp bands at 2950—3050 cm.$^{-1}$ associated with aromatic C–H stretching. If the silanols possessed ≥SiOH groups, the O–H band is shifted to *ca.* 3000 cm.$^{-1}$ (with weakening of intensity), and is thus masked by these C–H bands. This shift would result only if strong intramolecular bonding occurred, and it appears therefore that, for example, the silanol (VII; R = Me, R′ = H) has the structure (IXA or B).



(IXA)



(IXB)

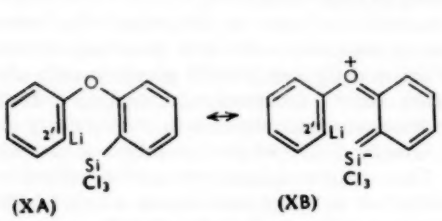
This intramolecular bonding would persist in solution, and the silanol does give a normal molecular weight in ethylene dibromide and in acetone. It would also account for the high stability of these compounds and in particular the absence of hydroxyl reactions.

The factors which determine the formation of these silanols are necessarily obscure, particularly as each silanol represents solely the one component which has been isolated in a pure condition from the initial crude mixture of products.

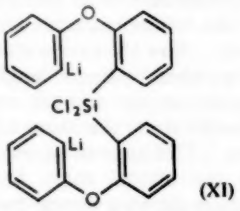
The following points regarding the possible mechanism of the reactions are tentatively suggested. The first stage in the formation of the unsubstituted spiran (IV) is the interaction of 2 : 2′-dilithiodiphenyl ether and silicon tetrachloride to form the 2′-lithio-derivative (XA) of trichloro-*o*-phenoxyphenylsilane, a process which occurs essentially by the interaction of the groups $\overset{-}{Cl}\text{–}\overset{+}{Si}\leq$ and $\geq\overset{-}{C}\text{–}\overset{+}{Li}$. The derivative (XA), however, receives some contribution from the polar form (XB), in which the silicon atom gains some negative character at the expense of the *o*-phenylene group and thus of the oxygen atom, and in turn of the 2′-carbon atom, which consequently becomes slightly deactivated. The next stage is thus the reaction of (XA–B) with another molecule of 2 : 2′-dilithiodiphenyl ether, whose carbanion reactivity is still unimpaired, with the formation of the dichlorodilithiosilane (XI), since this reaction is more rapid than the intramolecular reaction of (XA–B) to form 10 : 10-dichlorophenoxsilane. The final stage is the slower reaction of the silicon with the two 2′-carbon atoms in (XI) to give the spiran (IV), this intramolecular reaction being now favoured by the increasingly sterically shielded condition of the silicon atom.

[20] Kross, Fassel, and Margoshes, *J. Amer. Chem. Soc.*, 1956, **78**, 1332.
[21] Richards and Thompson, *J.*, 1949, 124.

When, however, silicon tetrachloride reacts with 2 : 2′-dilithio-5-methyldiphenyl ether (I; R = H, R′ = Me), the methyl group will activate the 2-carbon atom in the *para*-position and facilitate the formation of the initial trichloro-derivative (XIIA). In this compound, the 2′-carbon atom will be slightly deactivated by the polar form of type (XB),



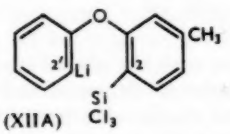
(XA) (XB)



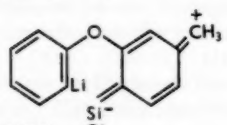
(XI)

and the silicon will have an increased negative contribution by the form (XIIC). Hence, as before, the most rapid reaction of (XII) is with another molecule of 2 : 2′-dilithio-5-methyldiphenyl ether (I; R = H, R′ = Me) to give the dichlorodilithio-derivative (XIII). The much increased negative contribution to the silicon now makes further reaction difficult, and prolonged boiling of the reaction mixture is required to induce some further cyclisation to the monochloro-derivative (XIV), which then undergoes no further cyclisation. There results a mixture of products, from which, during the subsequent working up, the small proportion of the monochloro-derivative (XIV) becomes hydrolysed to the silanol (VII; R = H, R′ = Me).

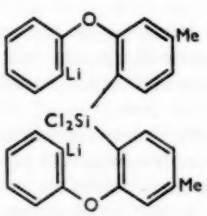
When 2 : 2′-dilithio-4-methyldiphenyl ether (I; R = Me, R′ = H) is used, the same factors enter, but the influence of the methyl group, now *meta* to the silicon, is much weaker. Consequently, the silicon in the dichloro-derivative (as XIII) is less deactivated, and further cyclisation to the monochloro-derivative (as XIV) occurs more readily, and a much higher yield of the silanol results.



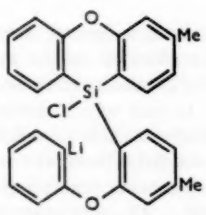
(XIIA)



(XIIC)



(XIII)



(XIV)

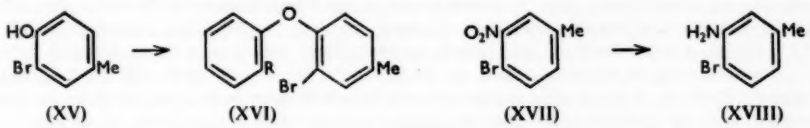
In view of the above results, the elucidation of the stereochemistry of the phenoxsilane system by *X*-ray crystal analysis appears to be the most promising.

Preparation of Intermediate Compounds.—For the above investigation 2 : 2′-dibromodiphenyl ether and certain methyl derivatives were required for the preparation of their dilithio-derivatives.

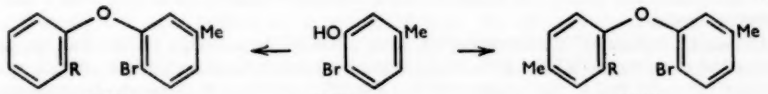
2 : 2′-Dibromodiphenyl ether was prepared from 2-amino-2′-bromodiphenyl ether by Mann and Millar's method.[1] 2 : 2′-Dibromo-4-methyldiphenyl ether (XVI; R = Br) was prepared by Campbell's method,[22] 3-bromo-4-hydroxytoluene (XV)[23] being condensed with *o*-chloronitrobenzene to give 2-bromo-4-methyl-2′-nitrodiphenyl ether (XVI; R = NO_2), which was converted into the 2′-amino-derivative (XVI; R = NH_2) and then into the 2′-bromo-derivative (XVI; R = Br).

[22] Campbell, *J.*, 1947, 4.
[23] Zincke and Wiederhold, *Annalen*, 1902, **320**, 199.

For the preparation of 2 : 2′-dibromo-5-methyldiphenyl ether (XIX; R = Br), 4-bromo-3-nitrotoluene (XVII) [24] was reduced with iron filings and aqueous sodium chloride to 3-amino-4-bromotoluene (XVIII), which was then converted into 4-bromo-3-hydroxytoluene (XX).[25] The latter, when condensed with *o*-chloronitrobenzene, gave 2-bromo-5-methyl-2′-nitrodiphenyl ether (XIX; R = NO_2), which by the usual stages afforded the 2 : 2′-dibromo-derivative (XIX; R = Br).



(XV) (XVI) (XVII) (XVIII)



(XIX) (XX) (XXI)

4-Bromo-3-hydroxytoluene (XX), when also condensed with 4-chloro-3-nitrotoluene, afforded 2-bromo-4′ : 5-dimethyl-2′-nitrodiphenyl ether (XXI; R = NO_2), which by similar stages gave 2 : 2′-dibromo-4 : 5′-dimethyldiphenyl ether (XXI; R = Br).

Experimental

The percentage yields obtained in the preparation of the phenoxsilanes are based on the weight of 2 : 2′-dibromodiphenyl ether (or its derivative) employed.

3-Amino-4-bromotoluene (XVIII).—A suspension of fine iron filings (250 g.) in 5% aqueous sodium chloride (1·25 l.) was boiled under reflux with vigorous stirring for 30 min. 4-Bromo-3-nitrotoluene (XVII) (125 g.) was then slowly added to the mixture, and the boiling continued for a further 3—4 hr. Steam-distillation and ether-extraction then gave the amine (XVIII) in 90% yield. Hodgson and Moore,[25] using tin and hydrochloric acid, obtained the amine in unspecified yield.

2-Bromo-5-methyl-2′-nitrodiphenyl ether (XIX; R = NO_2).—This was prepared essentially by Henley's method,[26] a mixture of 3-hydroxy-4-bromotoluene (XX) (93 g.), powdered potassium hydroxide (28 g., 1 mol.), and water (0·9 g., 0·1 mol.) being heated under an air-condenser in an oil-bath until homogeneous, and *o*-chloronitrobenzene (79 g., 1 mol.) then added during 5 min. The mixture was heated at 195—200° for 75 min., and poured into 7·5% aqueous potassium hydroxide (300 c.c.). The precipitated *2′-nitro-ether* (XIX; R = NO_2), when collected, dried, and distilled (63% yield), had b. p. 188—191°/0·7 mm., and m. p. 75—76° after crystallisation from ethanol (Found: C, 50·5; H, 3·1. $C_{13}H_{10}O_3NBr$ requires C, 50·7; H, 3·2%).

This nitro-ether was reduced by Campbell's method,[22] a mixture of the ether (XIX; R = NO_2) (106 g.), iron " pin-dust " (125 g.), and 50% aqueous ethanol being stirred and boiled under reflux whilst 48% hydrobromic acid (35 c.c.) was slowly added. After 3 hours' boiling, " Hyflo supercel " was added, and the mixture basified with 40% aqueous potassium hydroxide and filtered whilst hot. The residue, and the filtrate after dilution with water, were extracted with ether. Distillation gave the *2′-amino-ether* (XIX; R = NH_2) (58%), b. p. 168—170°/0·8 mm., 148·5—149·5°/0·3 mm. (Found: C, 56·1; H, 4·3. $C_{13}H_{12}ONBr$ requires C, 56·1; H, 4·3%). It gave a *benzoyl derivative* (XIX; R = NHBz), m. p. 102—104° (from aqueous ethanol) (Found: C, 62·9; H, 4·3. $C_{20}H_{16}O_2NBr$ requires C, 62·8; H, 4·2%), and an *acetyl derivative*, m. p. 92—93° when similarly recrystallised (Found: C, 55·7; H, 4·2. $C_{15}H_{14}O_2NBr$ requires C, 56·3; H, 4·4%).

The 2′-amino-ether (XIX; R = NH_2) (19 g.) was dissolved in a hot stirred mixture of 48% hydrobromic acid (150 c.c.) and water (150 c.c.), which was quickly cooled to *ca.* 5° by the addition of ice (*ca.* 300 g.). The suspension was diazotised with sodium nitrite (5·2 g., 1·1

[24] Gibson and Johnson, *J.*, 1929, 1229.
[25] Hodgson and Moore, *J.*, 1926, 2036.
[26] Henley, *J.*, 1930, 1222.

XUM

mols.), filtered, and then vigorously stirred whilst bromine (12·0 g., 1·1 mols.) in 48% hydrobromic acid (40 c.c.) was added dropwise, the temperature being kept below 10°. The precipitated yellow perbromide was collected, washed with ice-water, and added in small portions to acetic acid at 105°. The solution was boiled under reflux for 30 min., then poured into cold water, and the resulting suspension extracted with chloroform. The extract was washed with 20% aqueous potassium hydroxide and with water and dried. Distillation at 0·4 mm. gave fractions (*a*) b. p. 135—144°, (*b*) b. p. 144—170°, (*c*) b. p. 170—180°. Fraction (*a*) was discarded. Fraction (*b*) on redistillation gave 2 : 2′-*dibromo-5-methyldiphenyl ether* (XIX; R = Br) (13·3 g., 57%), b. p. 156—158°/0·4 mm. (Found: C, 45·6; H, 2·9. $C_{13}H_{10}OBr_2$ requires C, 45·6; H, 2·9%). Fraction (*c*) solidified, and when recrystallised four times from ethanol afforded 2 : 2′ : *x-tribromo-5-methyldiphenyl ether*, m. p. 62—64° (Found: C, 36·9; H, 2·4. $C_{13}H_9OBr_3$ requires C, 37·1; H, 2·1%); this compound was unaffected by hot aqueous-ethanolic sodium hydroxide, and the third bromine atom is almost certainly also in the aromatic nucleus.

The dibromo-ether (XIX; R = Br) was also obtained in 25% yield from the amine by the Sandmeyer method.

2-*Bromo-4′* : 5-*dimethyl-2′-nitrodiphenyl ether* (XXI; R = NO_2).—This was prepared as the 5-methyl compound (XIX; R = NO_2), from 4-bromo-3-hydroxytoluene (93 g.), potassium hydroxide (28 g., 1 mol.), and water (0·9 g., 1 mol.), and then 4-chloro-3-nitrotoluene (87 g., 1 mol.). Distillation gave the 2′-*nitro-ether* (XXI; R = NO_2), b. p. 175—179°/0·5 mm., m. p. 98—100° after crystallisation from ethanol (Found: C, 52·5; H, 3·7. $C_{14}H_{12}O_3NBr$ requires C, 52·2; H, 3·7%).

Reduction of this compound with " pin-dust " and hydrobromic acid gave the 2′-*amino-ether* (XXI; R = NH_2) (71%), b. p. 160—161°/0·7 mm., m. p. 32—35° (Found; C, 57·6; H, 4·5. $C_{14}H_{14}ONBr$ requires C, 57·6; H, 4·8%). The *benzoyl derivative* had m. p. 108—110° (from ethanol) (Found: C, 63·8; H, 4·5. $C_{21}H_{18}O_2NBr$ requires C, 63·7; H, 4·5%).

This amino-ether was converted by the Sandmeyer reaction, followed by distillation, into 2 : 2′-*dibromo-4* : 5′-*dimethyldiphenyl ether* (XXI; R = Br) (42%), b. p. 165—167°/0·5 mm., m. p. 85—86° (from ethanol) (Found: C, 47·0; H, 3·4. $C_{14}H_{12}OBr_2$ requires C, 47·2; H, 3·4%).

The preparation of the dibromo-ether (XXI; R = Br) by the above perbromide reaction gave considerable nuclear bromination and was abandoned.

A solution of *n*-butyl-lithium in light petroleum (b. p. 40—60°) was prepared by the method of Gilman and his co-workers [27] and standardised before use.

10 : 10-*Disubstituted Phenoxsilanes. General Method.*—The above solution of *n*-butyl-lithium (2·2 mols.) was added to a stirred solution of 2 : 2′-dibromodiphenyl ether (1 mol.) in light petroleum (b. p. 40—60°) or in ether under nitrogen, and the mixture boiled under reflux for 2 hr. The chloro-silane (1·2 mols.) in ether was then added to the hot stirred solution, which was next boiled under reflux for 3 hr. The chilled product was treated with water, and the organic layer separated, dried, and worked up as stated below.

(i) *Dichlorodimethyl-silane.* The organic layer on distillation gave 10 : 10-dimethylphenoxsilane (78%), b. p. 159—161°/9 mm., m. p. 74·5—77° after crystallisation from ethanol (Found: C, 74·2; H, 6·3. Calc. for $C_{14}H_{14}OSi$: C, 74·3; H, 6·2%) (lit.[3] m. p. 78·5—79°).

(ii) *Dichlorodiphenyl-silane.* (*a*) Use of a solution of 2 : 2′-dibromodiphenyl ether in the petroleum, and evaporation of the organic layer, gave a pale brown solid which on crystallisation from ethanol gave the 10 : 10-diphenylphenoxsilane (III; R = R′ = H) (59%), m. p. 175—177°, unchanged by recrystallisation from the petroleum or by sublimation at 200°/0·5 mm. (Found; C, 82·0; H, 4·9%; *M*, in boiling acetone, 360. Calc. for $C_{24}H_{18}OSi$; C, 82·2; H, 5·2%; *M*, 350) (lit.,[3] m. p. 178—179°).

(*b*) 2 : 2′-Dibromo-4-methyldiphenyl ether gave 2-*methyl*-10 : 10-*diphenylphenoxsilane* (III; R = Me, R′ = H), m. p. 153—155°, after crystallisation from the petroleum and sublimation at 160°/0·001 mm. (Found: C, 82·2; H, 5·6. $C_{25}H_{20}OSi$ requires C, 82·4; H, 5·5%) (yield of pure material, 55% of additional recovered material, 6%).

(*c*) An ethereal solution of 2 : 2′-dibromo-5-methyldiphenyl ether similarly gave 3-*methyl*-10 : 10-*diphenylphenoxsilane* (III; R = H, R′ = Me), m. p. 161—162°, after crystallisation and sublimation as before (Found: C, 82·2; H, 5·9. $C_{25}H_{20}OSi$ requires C, 82·4; H, 5·5%) (yield of pure material, 43%).

(*d*) 2 : 2′-Dibromo-4 : 5′-dimethyldiphenyl ether (XXI; R = Br) gave, on evaporation of the organic layer, a pale brown sticky residue, which after recrystallisation from the petroleum gave

[27] Gilman, Langham, and Moore, *J. Amer. Chem. Soc.*, 1940, **62**, 2327.

2 : 7-*dimethyl*-10 : 10-*diphenylphenoxsilane* (V) (46%), m. p. 155—161°, increased to 166—168° by recrystallisation from acetic acid, and then not affected by subsequent recrystallisation from the petroleum or by sublimation at 170°/0·001 mm. (Found: C, 82·4; H, 5·8. $C_{26}H_{22}OSi$ requires C, 82·6; H, 5·8%).

Derivatives of 2-*Methyl*-10 : 10-*diphenylphenoxsilane* (III; R = Me, R′ = H).—*N*-Bromosuccinimide (1·0 g., 1 mol.) was added to a solution of the silane (2·1 g.) in carbon tetrachloride (50 c.c.), which was boiled under reflux for 2 hr. Deposited succinimide (0·55 g.) was collected from the cold solution, which was then evaporated to dryness. The residue, when recrystallised from light petroleum (b. p. 60—80°) gave the 2-*bromomethyl-silane* (III; R = CH_2Br, R′ = H) (93%), m. p. 131·5—132° (decomp.) (from ethyl acetate) (Found: C, 67·5; H, 4·7. $C_{25}H_{19}OBrSi$ requires C, 67·7; H, 4·3%).

The use of *N*-bromosuccinimide (2·2 mols.) with a trace of benzoyl peroxide afforded, on evaporation of the solution, the 2-dibromomethyl-silane (III; R = $CHBr_2$, R′ = H) as a pale brown gum. Its solution in boiling 2-ethoxyethanol was therefore treated with aqueous silver nitrate (3·2 mols.) and, after boiling for a further 30 min., the solution was cooled and filtered into water, depositing the gummy 2-aldehydo-silane (III; R = CHO, R′ = H). This aldehyde did not crystallise, but in ethanolic solution gave an immediate copious red precipitate of the 2 : 4-*dinitrophenylhydrazone* [III; R = $CH{:}N{\cdot}NH{\cdot}C_6H_3(NO_2)_2$, R′ = H], m. p. 286—288° (decomp.) (from much acetic acid) (Found: C, 66·1; H, 4·8; N, 10·5. $C_{31}H_{22}O_5N_4Si$ requires C, 66·6; H, 4·0; N, 10·0%), very slightly soluble in the usual solvents.

spiro*Bis*-10-*phenoxsilane* (IV).—A solution of *n*-butyl-lithium (3·2 g., 2·2 mols.) in light petroleum (b. p. 40—45°) (50 c.c.) was added rapidly under nitrogen to a stirred solution of 2 : 2′-dibromodiphenyl ether (7·7 g.) in the petroleum (100 c.c.), which was boiled under reflux for 1 hr. The heating was stopped and a solution of silicon tetrachloride (4·3 g., 1·1 mols.) in ether (265 c.c.) rapidly added to the stirred mixture, which, after the vigorous reaction had ceased, was boiled for 3 hr. The solvent was removed, and the residue extracted under nitrogen with pure dioxan (Soxhlet). The extract, when concentrated and cooled, deposited crystals (2·5 g.), and no further crystalline material was obtained from the mother-liquors. The crystals, when sublimed at 280°/0·4 mm., gave the crude silane (IV) (61%), m. p. 255—271°, increased to 280—282° by recrystallisation from carbon tetrachloride or acetone (Found: C, 78·7; H, 4·5%; *M*, in freezing ethylene dibromide, 360. Calc. for $C_{24}H_{16}O_2Si$; C, 79·1; H, 4·4%; *M*, 364).

In a similar experiment, the 2 : 2′-dibromodiphenyl ether was used in ethereal solution, silicon tetrachloride (0·7 mol.) was added, and the final reaction mixture was cooled and hydrolysed with water. The white precipitate was collected, dried, and extracted with chloroform, which on concentration afforded the silane (IV), m. p. 280—282°, in 30% yield (Found: C, 78·8; H, 4·3%), a further 17% being recovered from the total organic liquors.

The Silanol (?VII; R = Me, R′ = H).—2 : 2′-Dibromo-4-methyldiphenyl ether (XVI; R = Br) (57 g.) in ether (300 c.c.) was lithiated under nitrogen with *n*-butyl-lithium (2·2 mols.) in light petroleum (b. p. 40—60°) (176 c.c.), treated with silicon tetrachloride (15·5 g., 0·55 mol.) in ether (100 c.c.), and boiled under reflux for 4 hr. The cold stirred solution was hydrolysed with water (50 c.c.), and the organic layer dried and distilled. The viscous residue, when crystallised from light petroleum (b. p. 60—80°), gave the *silanol* (5·7 g., 17%, including a second crop from the mother liquors), which when again recrystallised and then sublimed at 260°/0·1 mm. had m. p. 177—182° (Found: C, 75·9; H, 5·6%. $C_{24}H_{22}O_3Si$ requires C, 76·1; H, 5·4%; *M*, 410), and when then recrystallised from acetic acid and resublimed had m. p. 198—200° (Found: C, 75·9; H, 5·3%; *M*, in freezing ethylene dibromide, 380, in boiling acetone, 420).

The silanol (1·2 g.), when treated in carbon tetrachloride solution (50 c.c.) with *N*-bromosuccinimide (1·2 g., 2·2 mols.) and benzoyl peroxide (*ca.* 50 mg.) with subsequent boiling for 2 hr., deposited succinimide (0·65 g., *ca.* 100%). The filtrate on evaporation left a yellow glass, which when crystallised from acetic acid and ethyl acetate gave the white *di*-(2-*bromomethyl*)-*silanol* (?VII; R = CH_2Br, R′ = H) (0·6 g., 43%), m. p. 168—171° (decomp.) (Found: C, 55·1; H, 3·6. $C_{26}H_{20}O_3Br_2Si$ requires C, 55·0; H, 3·5%). A solution of this compound (3·8 g.) in chloroform (30 c.c.) was treated with a saturated chloroform solution of hexamethylenetetramine (2·1 g., 2·1 mols.) and boiled under reflux for 2 hr., cooled, and filtered. The collected hexaminium salt (4·9 g., 85%) had m. p. 175—180° (decomp.). A mixture of this salt (0·5 g.) and 50% aqueous acetic acid (7 c.c.) was heated under reflux at 145° for 70 min., diluted with

concentrated hydrochloric acid (5 c.c.), and boiled for 5 min. The cold suspension, when collected and recrystallised from acetic acid gave the *di-(2-aldehydo)-silanol* (?VII; R = CHO, R′ = H) (0·1 g., 40%), m. p. 230—231° (Found: C, 71·3; H, 4·1. $C_{26}H_{18}O_5Si$ requires C, 71·3; H, 4·1%). The infrared spectra of these two derivatives gave no indication of a hydroxyl group.

The Silanol (?VII; R = H, R′ = Me).—This compound was prepared as the previous silanol, and evaporation of the organic layer gave a viscous residue which when twice recrystallised from acetic acid and sublimed at 210°/0·001 mm. gave the crude white silanol (4%), m. p. 200—210°. Repeated alternate crystallisation from acetic acid and sublimation ultimately gave the pure *silanol*, m. p. 215—217° (Found: C, 75·9; H, 5·2%; *M*, in freezing benzene, 390. $C_{26}H_{22}O_3Si$ requires C, 76·1; H, 5·4%; *M*, 410).

Dipole moments.

10 : 10-*Diphenylphenoxsilane* (III; R = R′ = H)

w	ε	*v*	*n*
0·010378	2·2804	1·1414	0·00142
0·008806	2·2790	—	—
0·008462	2·2787	1·1420	0·00112
0·006455	2·2776	1·1427	0·00083
0·003712	2·2753	1·1435	0·00043
0·002332	2·2747	1·1440	0·00024
0·002225	2·2745	—	—

$\epsilon = 2{\cdot}2728 + 0{\cdot}714w$; $v = 1{\cdot}1447 - 0{\cdot}321w$; $\Delta n_D = -0{\cdot}00011 + 0{\cdot}147w$; $\mu = 0{\cdot}97 \pm 0{\cdot}03$ D; ${}_EP = 114{\cdot}10$ c.c. ${}_TP = 133{\cdot}2$ c.c.

2 : 7-*Dimethyl*-10 : 10-*diphenylphenoxsilane* (V)

w	ε	*v*	*n*
0·008638	2·2785		
0·007044	2·2772		
0·006213	2·2768		
0·005552	2·2764		
0·004349	2·2755		
0·003026	2·2744		
0·002125	2·2741		
0·008708	—	1·1420	0·00113
0·007470	—	1·1424	0·00095
0·005965	—	1·1429	0·00073
0·004590	—	1·1433	0·00058
0·001723	—	1·1440	0·00020

$\epsilon = 2{\cdot}2727 + 0{\cdot}670w$; $v = 1{\cdot}1445 + 0{\cdot}284w$; $\Delta n_D = -0{\cdot}00003 + 0{\cdot}132w$; $\mu = 1{\cdot}01 \pm 0{\cdot}03$ D; ${}_EP = 124{\cdot}08$ c.c.; ${}_TP = 144{\cdot}87$ c.c.

Dipole Moments.—The determinations (see Table) were carried out in benzene at 25°. The symbol *w* represents weight fraction of solute in benzene, ε the dielectric constant of solution, *v* the specific volume of solution, and Δn_D the refractive-index difference between solution and benzene for Na_D light.

The equations show the rectilinear relation between ε, *v*, and Δn_D, respectively, and *w*.

The Halverstadt–Kumler treatment [28] was used to determine the dipole moments, μ, and the electronic polarisations at infinite dilution ${}_EP$. The differences are $\Delta\mu = 0{\cdot}09 \pm 0{\cdot}06$ D; $\Delta_EP = 9{\cdot}98$ c.c. The difference between the electronic polarisations agrees as well as can be expected with the value for two CH_2 groups given in Landolt and Börnstein's Tables, *viz.*, 9·23 c.c. No allowance has been made for ${}_AP$ other than that implicit in using $[R]_D$ as the distortion polarisation.

We are greatly indebted to Mr. E. W. Randall and Dr. L. E. Sutton, F.R.S., for the determination and analysis of the above dipole moments, and to the Department of Scientific and Industrial Research and the Wellcome Trust for grants (to C. H. S. Hitchcock and A. Vanterpool respectively).

University Chemical Laboratory, Cambridge. [*Received, June 5th*, 1957.]

[28] Halverstadt and Kumler, *J. Amer. Chem. Soc.*, 1942, **64**, 2988.

914. *Oxidation of Organic Sulphides. Part IX.* The Reaction of Ozone with Organic Sulphur Compounds.†*

By D. Barnard.

Organic monosulphides are oxidised by somewhat less than the theoretical amount of ozone, to give high yields of the respective sulphone *via* the sulphoxide. Disulphides undergo a more complex reaction, giving the sulphonic anhydride as the major product and smaller amounts of thiol-sulphonate and disulphone. Tetrasulphides also give sulphonic anhydride in high yield, together with sulphur dioxide. Reaction mechanisms are suggested based upon ozone-absorption measurements, the effect of ozone on related sulphur compounds, and rate data derived from competitive ozonolyses.

Ozonolytic degradation of natural rubber and related polymers is generally attributed to the interaction of ozone with the double bonds of the polyisoprenic chains. Where rubber has been vulcanised with sulphur, other potential sites of attack are available to the ozone, namely, the cross-links formed in the vulcanisation process and composed of chains of from one to five sulphur atoms. This work describes the reactions of ozone with such groups in model mono-, di-, and poly-sulphides and some related compounds.

The experimental procedure was to pass an accurately controlled stream of ozonised

Fig. 1. *Ozonolysis of (a) carbon tetrachloride (50 ml.) and (b) di-n-butyl sulphide (2 g.) in carbon tetrachloride.*

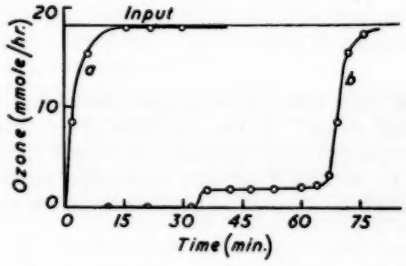
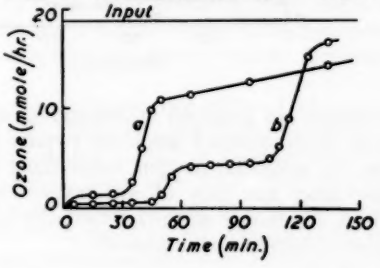


Fig. 2. *Ozonolysis of (a) diphenyl sulphide (2 g.) and (b) methyl phenyl sulphide (2 g.).*



oxygen (*ca.* 0·3 mmole of ozone/min.) through a 1—3% solution of the compound at −25° in a reaction vessel similar to that described by Boer and Kooyman.[1] Carbon tetrachloride or, where a more polar solvent was necessary, carbon tetrachloride–nitromethane (1 : 3 v/v) were satisfactory solvents, allowing 98—99% of the ozone to pass through unchanged with no solute present. By periodic analysis of the exit gas stream an uptake curve was plotted from which the absorption of ozone could be derived with an accuracy of *ca.* ±3%, as determined by calibration with pure olefins. Large differences in rates of ozonolysis were visible from these curves but the determination of relative rates, where possible, had to be made by a competitive method. Product analyses were performed either at the end or at intermediate stages of the ozonolysis.

Monosulphides.—Monosulphides are oxidised to sulphones by an excess of ozone.[2] Uptake curves for some representative examples are given in Figs. 1 and 2. The yield of sulphones was 90—100%, traces of the appropriate aldehyde and acid indicating some concomitant C–S bond fission. The uptake curves show that oxidation occurs in two

* Part VIII, Bateman, Cunneen, and Ford, *J.*, 1957, 1539.
† Presented, in part, at the 14th Internat. Congr., Union Pure Appl. Chem., Zürich, 1955.

[1] Boer and Kooyman, *Analyt. Chim. Acta*, 1951, **5**, 550.
[2] Böhme and Fischer, *Ber.*, 1942, **75**, 1310.

well-defined stages to give, first, the sulphoxide and then the sulphone. By using a flowing cell device [3] to follow the ozonolysis of *cyclo*hexyl methyl sulphide by infrared spectroscopy, at least 98—99% of the sulphide was found to be converted into sulphoxide before any sulphone was detected, indicating a minimum factor of 50—100 between the rates of the two stages. The reactivity of the sulphides decreases with the introduction of aryl groups: diphenyl sulphoxide is so resistant to further oxidation that it is difficult to obtain diphenyl sulphone free from sulphoxide (Böhme and Fischer [2] record similar behaviour with chloromethyl ethyl sulphide). These observations are in accord with considerations of electron-availability at the sulphur atom. Competitive ozonolyses indicated that oct-1-ene reacts with ozone at least 50 times more rapidly than does di-*n*-butyl sulphide which was the most easily oxidised of the sulphides investigated.

The reaction

$$R'\cdot S\cdot R'' + 2O_3 \longrightarrow R'\cdot SO_2\cdot R'' + 2O_2$$

was found not to be quantitatively followed, less than the theoretical amount of ozone being required for a virtually quantitative yield of sulphone. Table 1, in which the sulphides are arranged in descending order of their rates of ozonolysis, shows that the most easily oxidised sulphides require the least ozone. As the sulphides are normally inert to molecular oxygen, ozone must either catalyse their oxidation by oxygen or give rise, after the loss of an oxygen atom, to activated oxygen molecules some of which, depending on the oxidisability of the sulphide, themselves participate in the oxidation of sulphide or sulphoxide.

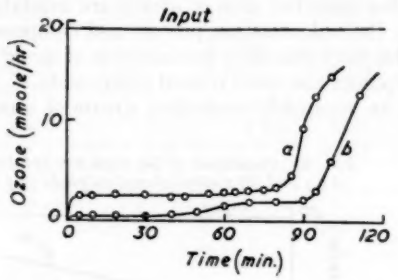


FIG. 3. *Ozonolysis of (a) diphenyl disulphide (2 g.) and (b) di-n-butyl disulphide (2 g.).*

TABLE 1. *Ozone required for sulphone formation.*

Sulphide	Ozone (mol.)	Sulphide	Ozone (mol.)
Di-*n*-butyl	1·40	Dibenzyl	1·75
*cyclo*Hexyl methyl	1·53	Methyl phenyl	1·85
2-Ethyl-2-methyl-5-*iso*propylthiophan	1·70	Diphenyl	1·03 *

* To sulphoxide.

Disulphides.—By analogy with the oxidation of monosulphides, disulphides would be expected to yield successively thiolsulphinate, R·SO·S·R, thiolsulphonate, $R\cdot SO_2\cdot S\cdot R$, or disulphoxide, R·SO·SO·R, and disulphone, $R\cdot SO_2\cdot SO_2\cdot R$. Ozone-uptake curves (cf. Fig. 3) did not reveal such stepwise reaction and indicated, for "normal" disulphides, the absorption of a 2·5—3 mols. of ozone (cf. Table 2). The crude products contained *ca.* 5 oxygen atoms for each original disulphide molecule and dissolved almost completely in water to give the corresponding sulphonic acid. Their infrared spectra showed the initial absence of hydroxyl groups, but strong absorption at *ca.* 1400 and 1190 $cm.^{-1}$ suggested the presence of the $R\cdot SO_2\cdot O$ group, and the identity of the major products as a sulphonic anhydride, $R\cdot SO_2\cdot O\cdot SO_2\cdot R$, was confirmed by their isolation. Yields of the anhydrides were conveniently measured by the titration of the acids produced on

[3] Higgins, unpublished work.

hydrolysis or by the comparison of the intensity of either of the above infrared absorption bands with calibration curves. For the small-scale preparation of sulphonic anhydrides ozonolysis of the appropriate disulphide appears to compare favourably with other methods available.[4]

Neutral products (after removal of the sulphonic anhydride) were purified chromatographically and shown to consist of the corresponding thiolsulphonate with traces of disulphone and unidentified material.

Dibenzyl disulphide gave no sulphonic anhydride: sulphur dioxide, sulphuric acid, benzaldehyde, and benzoic acid were identified as products. Dimethyl disulphide was also atypical in that methyl methanethiolsulphonate, and not methanesulphonic anhydride, was the major product.

TABLE 2. *Products of ozonolysis of disulphides,* R_2S_2.

R	O_3 absorbed (mols.)	Sulphonic anhydride (%)	Thiol-sulphonate (%)	R	O_3 absorbed (mols.)	Sulphonic anhydride (%)	Thiol-sulphonate (%)
Ph	2·6	90	6	Me	2·0	39	*ca.* 50
p-Cl·C_6H_4 ...	2·9	84	10	CH_2Ph	5	—	—
Bu[a]	2·6	80	*ca.* 10				

The ozonolysis of diphenyl disulphide was examined in greater detail. It was significant that *ca.* 3 molecules of ozone supply 5 atoms of oxygen; thus the reaction probably involves at least three steps, an ozone molecule being incorporated in one step with normal donation of oxygen to sulphur in the others. In agreement with this phenyl benzenethiolsulphinate, in which one sulphur atom has already acquired an oxygen atom, gave a high yield (87%) of benzenesulphonic anhydride when ozonised, each molecule receiving a further 4 oxygen atoms from *ca.* 2 molecules of ozone. Other thiolsulphinates behaved similarly. Nevertheless, thiolsulphinate is not an intermediate in the formation of sulphonic anhydride.

When diphenyl disulphide was treated with, for example two-fifths of the ozone required for complete conversion into sulphonic anhydride an intermediate containing two oxygen atoms per molecule was not found and only the normal products of complete ozonolysis of almost exactly two-fifths of the disulphide were identified. This suggests that the initial attack of ozone on the disulphide must be the slowest step of the overall reaction. It was shown that thiolsulphinate reacts with ozone at only two-thirds of the rate of the disulphide and since it could never be detected amongst the products of partial ozonolysis, although control experiments indicated that it was stable enough to survive the isolation procedure, it follows that it is not formed in significant amount by the oxidation of disulphide. Table 3 illustrates the results of differing degrees of ozonolysis of diphenyl

TABLE 3. *Partial ozonolysis of diphenyl disulphide.*

Ozonolysis (%)	Disulphide recovered (%)	Yield of sulphonic anhydride (%)	Yield of thiol-sulphonate (%)	Ozonolysis (%)	Disulphide recovered (%)	Yield of sulphonic anhydride (%)	Yield of thiol-sulphonate (%)
29	63	48	32	49	49	73	15
36	55	55	20	86	16	80	—
41	58	61	21	100	—	90	6
44	54	67	20				

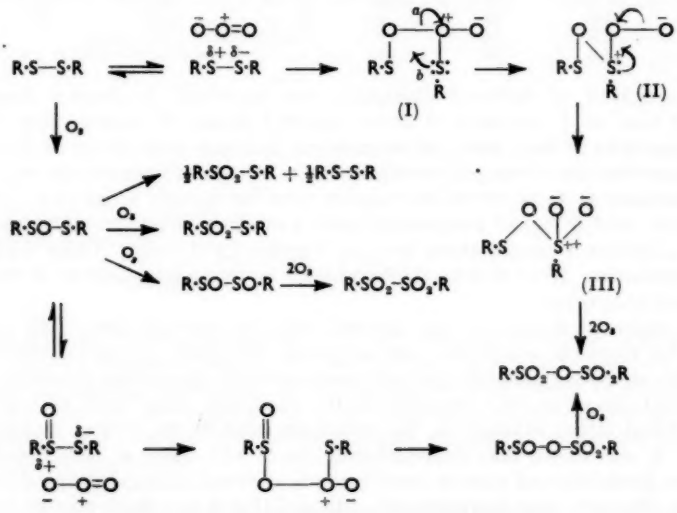
disulphide. At the lower extents of reaction the yield of thiolsulphonate is increased at the expense of sulphonic anhydride. This implies that virtually all the thiolsulphonate is formed at the onset of ozonolysis, the reason for which is not apparent. Wibaut and his co-workers [5] have found that Lewis acids catalyse the reaction of ozone with benzene

[4] Billeter, *Ber.*, 1905, **38**, 2015; Shepherd, *J. Org. Chem.*, 1947, **12**, 275; Field, *J. Amer. Chem. Soc.*, 1952, **74**, 394; Field and Settlage, *ibid.*, 1954, **76**, 1222; Owen and Whitelaw, *J.*, 1953, 3723; Standard Oil Co., B.P. 672,640.

[5] Wibaut, Sixma, Kampschmidt, and Boer, *Rec. Trav. chim.*, 1950, **69**, 1355.

and other aromatic hydrocarbons and it is possible that sulphonic anhydride formation becomes increasingly favoured as the reaction proceeds by the catalytic influence of the small amounts of sulphonic or sulphuric acids invariably present. Thiolsulphonate was shown to be inert to ozone under the reaction conditions, presumably owing to the electron-attracting effect of the sulphone group on the unoxidised sulphur atom. A formally similar deactivation was observed in thiol-esters. Thiolsulphonate added initially to disulphide was recovered completely after ozonolysis, together with the normal yield of thiolsulphonate and sulphonic anhydride from the disulphide, indicating that it did not participate in any stage of the reaction.

The reaction sequence in the annexed scheme appears to explain the known facts and bears a formal resemblance to the mechanism of ozonisation of olefins formulated by Criegee.[6] The disulphide, polarised by the approaching reagent, adds to an ozone molecule to give (I) which by rapid rearrangement yields (II) and (III), the last product being oxidised by a further 2 mols. of ozone (in view of the results with monosulphides only



1·6—1·8 mols. would probably be required) to the final product. The electron switches *a* and *b* in (I) are envisaged as sequential, the driving force for *b* being the great electron-affinity of the momentarily positively charged oxygen atom left by *a*. If the O–O bond cleavage were in part homolytic the R·S·O· radicals so formed could be the source of the thiolsulphonate since it has been shown [7] that this type of radical left after the abstraction of chlorine by zinc from sulphinyl chlorides readily undergoes the reaction

$$2R\cdot S\text{–}O\cdot \rightleftharpoons 2R\cdot \dot{S}{=}O \longrightarrow R\cdot SO_2\cdot S\cdot R$$

The accompanying $R\cdot SO_2\cdot$ radical could conceivably give rise to the small amounts of disulphone formed. Alternative sources of thiolsulphonate and disulphone are the disproportionation and asymmetrical or symmetrical oxidation of thiolsulphinate. However, the similarity of the yields of thiolsulphonate from ozonolysis of disulphide and thiolsulphinate would demand that almost the whole of the disulphide would have to react *via* the thiolsulphinate, and this, as has been shown, is not acceptable. The formation of sulphonic anhydride from (III) demands ready oxidation of the grouping R·S·O⁻. That

[6] Criegee, 120th Meeting Amer. Chem. Soc., Sept., 1951.
[7] Barnard, unpublished work.

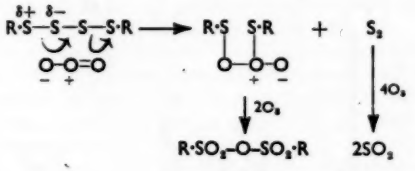
this occurs in a similar context was demonstrated by the conversion of 2 : 4-dinitrobenzenesulphenic anhydride into the sulphonic anhydride by ozone. Methyl benzenesulphenate was however oxidised only to methyl benzenesulphinate, and not to the sulphonate as would be expected.

Tetrasulphides.—Di*iso*propyl and di-*p*-chlorophenyl tetrasulphide, used as models, were both converted in high yield into the sulphonic anhydrides with the elimination of half the sulphur as sulphur dioxide. The uptake curves and detailed results are given in Fig. 4 and Table 4.

TABLE 4. *The reaction of ozone with tetrasulphides.*

Tetrasulphide	O_3 absorbed (mols.)	Sulphonic anhydride (%)	SO_2 (mols.)
Di*iso*propyl	6·0	83	2·1
Di-*p*-chlorophenyl	5·5	75	1·7

The mechanism of reaction is envisaged as being basically the same as that of disulphides except for the elimination and subsequent oxidation of the non-terminal sulphur atoms after the initial polarisation of the molecule.



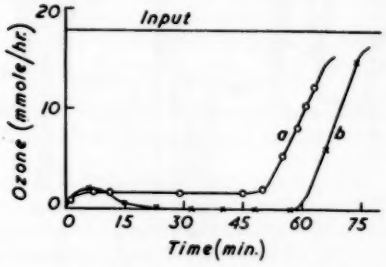


FIG. 4. *Ozonolysis of* (*a*) *di*iso*propyl tetrasulphide* (0·5 *g.*) *and* (*b*) *di*-p-*chlorophenyl tetrasulphide* (1 *g.*).

Miscellaneous Sulphur Compounds.—The results of the ozonolysis of sulphur compounds other than sulphides are summarised in Table 5.

TABLE 5. *The ozonolysis of miscellaneous sulphur compounds.*

Structure *	O_3 absorbed (mols.)	Product	Yield (%)
Ph·SO·SPh	1·7	Ph·SO_2·O·SO_2·Ph	85
R·S·O·SR †	4	R·SO_2·O·SO_2·R	*ca.* 100
Ph·SH	1·6	Ph·SO_2H	*ca.* 100
Ph·S·OMe	0·7	Ph·SO·OMe	*ca.* 100

* No ozone was absorbed by Ph·SO_2·SPh, Ph·SO_2·SO_2·Ph, or Bu^nS·COMe.
† R = 2 : 4-dinitrophenyl.

Rates of Ozonolysis.—The rapidity of the ozonolyses made conventional rate measurements impracticable and the relative rates given in Table 6 were derived from a series of ozonolyses in which di-*n*-butyl sulphide competed in turn with the other compounds for

TABLE 6. *Relative rates of ozonolysis.*

Ph·SO·SPh	Ph_2S_2	$Bu^n_2S_2$	Bu^n_2S	Oct-1-ene
1	1·6	2·5	99	*ca.* 5000

an insufficiency of ozone. Since the olefinic double bonds in rubber react with ozone more rapidly than the double bond in oct-1-ene,[7] the degradation by ozone of the polysulphide

cross-links in vulcanised rubber can be regarded as unimportant compared with the degradation of the rubber trunk chains.

Experimental

Fig. 5 illustrates the apparatus used. Oxygen from a cylinder passed through a chromic acid bubbler (not shown) to the pressure regulator *A* (filled with sulphuric acid), flowmeter *B*, and liquid-oxygen cooled trap *C* before reaching the silent-discharge ozoniser *D* which produced *ca.* 0·3 mmole of ozone per min. with a gas flow of 8 l./hr. The ozone stream could be led to the atmosphere, the analyser [1] *E*, or the reaction vessel *via* a three-way tap and the solenoid-operated, all-glass valve system *F*, the hydrostatic pressure head being adjusted in each case to maintain a constant flow. The valves were switched either manually or by a timer unit which accurately switched the gas stream between the reaction vessel and analyser (in cycles of 3 min. : 10 sec.) and were water-cooled. From the ozone estimated in the analyser the input of ozone to the reaction vessel during a given time could be calculated with the minimum of error

Fig. 5. *Ozonolysis apparatus.*

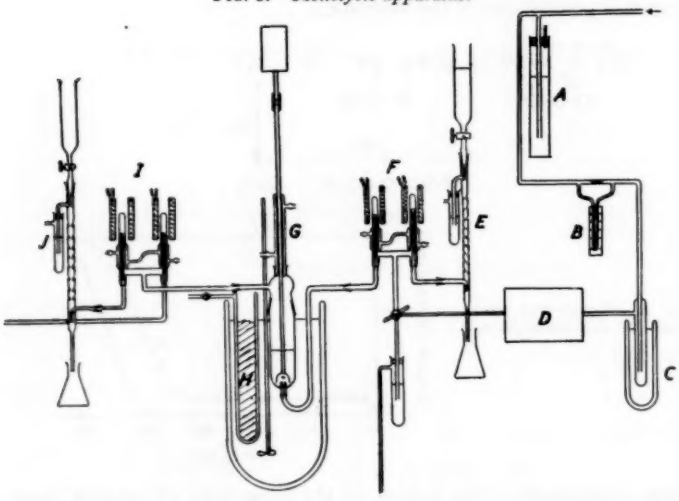


Fig. 6. *Vacuum-crystallisation apparatus.*

due to variations in the rate of ozone production. However, with the ozoniser in thermal equilibrium and with careful control of flow rates such variations were negligible (±1·5%) during a run of average duration (½—2 hr.). The precision-bore stirrer *G*, lubricated with Silicone oil, proved to be gas-tight under the small pressure differentials used, and the unsilvered Dewar flask *H*, filled with crushed, solid carbon dioxide, could be partially evacuated to maintain the ethanol (4 l.) in the large Dewar vessel at −25° ± 0·5° for several hours. The exit gas stream was led to ozone analysers *J* and *K* (not shown) *via* a second valve system *I* also controlled by the timing unit and switching in phase with the reaction vessel valve *F*. Taps and ground-glass joints were lightly lubricated with Silicone stopcock grease.

Solvents.—"AnalaR" carbon tetrachloride was further purified and dried by fractional distillation. Nitromethane was subjected to a preliminary ozonolysis for 6 hr. in the presence of water, dried ($CaCl_2$), and after fractional distillation had b. p. 100·6—101·0°/740 mm.

Sulphur Compounds.—These were purified commercial samples except for the following: The preparation and physical properties of *cyclo*hexyl methyl and methyl phenyl sulphide have been previously described.[8] Di-*p*-chlorophenyl disulphide and tetrasulphide were respectively prepared from *p*-chlorobenzenethiol by oxidation with alkaline hydrogen peroxide and condensation with sulphur monochloride. The disulphide had m. p. 70·8—71·2° (Found: C, 50·1; H, 2·8; Cl, 24·6; S, 22·2. Calc. for $C_{12}H_8Cl_2S_2$: C, 50·2; H, 2·8; Cl, 24·8; S, 22·3%) and

[8] Barnard, Fabian and Koch, *J.*, 1949, 2442.

the tetrasulphide had m. p. 21—25° (Found: C, 41·2; H, 2·3; S, 36·5. Calc. for $C_{12}H_8Cl_2S_4$: C, 41·0; H, 2·3; S, 36·5%). Phenyl benzenethiolsulphinate [9] had m. p. 69—70° (Found: C, 61·4; H, 4·2; S, 27·3. Calc. for $C_{12}H_{10}OS_2$: C, 61·5; H, 4·27; S, 27·4%). Phenyl benzenethiolsulphonate, obtained by the thermal decomposition of benzenesulphinic acid, had m. p. 37—38° (Found: C, 57·6; H, 4·1; S, 25·6. Calc. for $C_{12}H_{10}O_2S_2$: C, 57·6; H, 4·0; S, 25·6%). 2 : 4-Dinitrobenzenesulphenic anhydride [10] had m. p. 117—118° (decomp.) (Found: C, 34·6; H, 1·7. Calc. for $C_{12}H_6O_9N_4S_2$: C, 34·8; H, 1·5%). Methyl benzenesulphenate, synthesised by the reaction of methanol with benzenesulphenyl chloride,[11] had b. p. 54—55°/0·7 mm., n_D^{20} 1·5633 (Found: C, 60·2; H, 5·7; S, 22·8. Calc. for C_7H_8OS: C, 60·0; H, 5·7; S, 22·9%). Diphenyl disulphone, m. p. 191—192° (Found: C, 50·9; H, 3·5; S, 22·6. Calc. for $C_{12}H_{10}O_4S_2$: C, 51·0; H, 3·6; S, 22·7%), was obtained by the oxidation of benzenesulphinic acid with potassium permanganate.[12] Analytically pure samples of di*iso*propyl tetrasulphide and *n*-butyl thiolacetate were kindly presented by Dr. C. G. Moore and Mr. J. Ford respectively.

Ozonolysis of Monosulphides.—Samples (2 g.), ozonised just to completion, gave:

Di-*n*-butyl sulphone (2·47 g.), m. p. 41·5—43·5°, smelling of butyraldehyde and butyric acid and reacting acid to litmus (Found: C, 53·6; H, 9·75; S, 17·8. Calc. for $C_8H_{18}O_2S$: C, 53·95; H, 10·1; S, 18·0%). After one crystallisation from light petroleum (b. p. 60—80°) the m. p. and mixed m. p. of the product (2·0 g.) was 44—44·5°.

*cyclo*Hexyl methyl sulphone (2·50 g.), n_D^{20} 1·4912, b. p. 93·4°/0·04 mm. (Found: C, 51·7; H, 8·45; S, 19·7. Calc. for $C_7H_{14}O_2S$: C, 51·8; H, 8·7; S, 19·7%).

Dibenzyl sulphone (2·41 g.), m. p. 143—147°, acid to litmus and with an odour of benzaldehyde. The filtrate after washing of the crystals with ethanol (3 ml.) gave a small precipitate of benzaldehyde 2 : 4-dinitrophenylhydrazone, m. p. 236—236·5°, on treatment with Brady's reagent. The residue had m. p. and mixed m. p. 150·5—151·5° after one crystallisation from light petroleum (b. p. 60—80°)–chloroform.

Methyl phenyl sulphone (2·45 g.), m. p. 84—86°, which, after one crystallisation from light petroleum (b. p. 60—80°)–chloroform, had m. p. and mixed m. p. 86—86·5°.

2-Ethyl-2-methyl-5-*iso*propylthiophan 1 : 1-dioxide, a pale-red oil (2·60 g.) which after molecular distillation had n_D^{20} 1·4765 (Found: C, 58·3; H, 9·8; S, 15·3. Calc. for $C_{10}H_{20}O_2S$: C, 58·8; H, 9·8; S, 15·7%).

Diphenyl sulphone: no sample free from diphenyl sulphoxide was obtained. An increased time of ozonolysis lessened the amount of sulphoxide but produced more resinous by-products derived from attack on the benzene ring.

Ozonolysis of Disulphides.—Examination of diphenyl disulphide may be considered typical. The disulphide (2 g.) in nitromethane (50 ml.)–carbon tetrachloride (18 ml.) was ozonised to completion (*ca.* 90 min.) to give, after the removal of solvent *in vacuo*, a white crystalline residue which became red and oily. This decomposition could be prevented by the addition of anhydrous potassium carbonate (1 g.) before ozonolysis. The residue was transferred, *via* a dry box, to limb *A* of the vacuum-crystallisation apparatus (Fig. 6), and 1 : 1 anhydrous light petroleum (b. p. 30—40°)–ether (90 ml.) distilled *in vacuo* into the apparatus which was then sealed at *C*. The anhydride dissolved on warming to 40° and the solution was filtered into *B* where crystallisation occurred at −60°. The mother-liquor was filtered back into *A* and clean solvent distilled into *B*. After 4 crystallisations the anhydride was dried by cooling *A* in liquid air. The benzenesulphonic anhydride obtained (1·05 g.) had m. p. and mixed m. p. 91—92° (cf. Field [4]) (Found: C, 48·2; H, 3·4; S, 21·5%; equiv., 148·8. Calc. for $C_{12}H_{10}O_5S_2$: C, 48·35; H, 3·35; S, 21·5%; equiv., 149). The infrared spectrum with characteristic absorption at 1191 (ε 1185) and 1402 cm.$^{-1}$ (ε 797) was identical with that of the authentic specimen.

The residue from a similar ozonolysis in the absence of potassium carbonate was immediately dissolved in water (50 ml.), and the resulting sulphonic acid titrated with 0·1969N-alkali (84·2 ml., 90%) to screened methyl-red. After extraction with ether (2 × 50 ml.) and concentration to small volume (10 ml.) the solution was treated with *S*-benzylthiuronium chloride (4 g.) in water (14 ml.), to give the benzenesulphonate (3·76 g.), m. p. 139—141°, m. p. and mixed m. p. 146—147° after one crystallisation from light petroleum (b. p. 60—80°)–acetone. The ethereal extracts left a pale brown oil (0·3 g.) on evaporation. This was dissolved in

[9] Backer and Kloosterziel, *Rec. Trav. chim.*, 1954, **73**, 129.
[10] Kharasch, King, and Bruice, *J. Amer. Chem. Soc.*, 1955, **77**, 931.
[11] Lecher, *Ber.*, 1925, **58**, 409.
[12] Hilditch, *J.*, 1908, 1524.

carbon tetrachloride (25 ml.) and fractionally eluted from a column of silica gel (15 g., 100—200 mesh) with carbon tetrachloride (100 ml.) and then chloroform (100 + 50 ml.) to give diphenyl disulphide (10 mg.), phenyl benzenethiolsulphonate (0·17 g.), m. p. 34—35° [m. p. and mixed m. p. 37—38° after one crystallisation from light petroleum (b. p. 60—80°)–ethanol], and a brown oil (0·04 g.) which was identified by its infrared spectrum as impure diphenyl disulphone.

The products from the partial ozonolyses of diphenyl disulphide were estimated and identified as above.

Other ozonolyses gave the following products:

Di-p-chlorobenzenesulphonic anhydride, m. p. 148—149°, obtained in 84% yield (by titration), had strong absorption at 1196 (ε 1150) and 1415 cm.$^{-1}$ (ε 1090) (Found: C, 39·3; H, 2·2; Cl, 19·3; S, 16·9%; equiv., 184·9. $C_{12}H_8O_5Cl_2S_2$ requires C, 39·3; H, 2·2; Cl, 19·3; S, 17·4%; equiv., 183·5). Amongst the neutral products (0·21 g.) also obtained from disulphide (1 g.) were *p*-chlorophenyl *p*-chlorobenzenethiolsulphonate (0·11 g.), m. p. 177—178° (Found: C, 45·0; H, 2·5. Calc. for $C_{12}H_8O_2Cl_2S_2$: C, 45·1; H, 2·5%), and di-*p*-chlorophenyl disulphone (30 mg.), m. p. >230°, identified by its infrared spectrum (Found: C, 40·9; H, 2·5. Calc. for $C_{12}H_8O_4Cl_2S_2$: C, 41·0; H, 2·3%).

The oil (5·61 g.), obtained from the ozonolysis of dimethyl disulphide (4 g.), was separated by distillation into methyl methanethiolsulphonate (2·57 g.) and the anhydride (2·93 g.). The latter, after 3 crystallisations *in vacuo* from light petroleum (b. p. 30—40°)–ether, had m. p. 69—70° (Found: C, 13·7; H, 3·4; S, 37·0%; equiv., 86·2. Calc. for $C_2H_6O_5S_2$: C, 13·8; H, 3·45; S, 36·8%; equiv., 87·0) and strong absorption at 1187 (ε 1124) and 1391 cm.$^{-1}$ (ε 1100). The thiolsulphonate after refractionation had b. p. 104—105°/10 mm., n_D^{20} 1·5128 (Found: C, 19·2; H, 4·8; S, 50·5. Calc. for $C_2H_6O_2S_2$: C, 19·1; H, 4·8; S, 50·8%), with absorption at 1141 (ε 724) and 1343 cm.$^{-1}$ (ε 554).

n-Butanesulphonic anhydride (1·35 g.), obtained from di-*n*-butyl disulphide (1 g.), had a purity of 85% (by titration) as anhydride and rapidly darkened. The purity was not raised by molecular distillation at 85°/10^{-3} mm. (Found: C, 37·0; H, 7·25; S, 24·5. Calc. for $C_8H_{18}O_5S_2$: C, 37·2; H, 6·98; S, 24·8%). The product contained *ca.* 10% of thiolsulphonate (infrared spectroscopy with methyl methanethiolsulphonate as standard).

Ozonolysis of Tetrasulphides.—This was carried out as for the disulphides except that the whole, or a part, of the exit gas stream was led through standard sodium hydroxide solution. Sulphur dioxide was converted into sodium sulphite and then by the ozone present into sodium sulphate and was estimated by back-titration of the alkali or gravimetrically as benzidine sulphate. Only traces of sulphur trioxide were detected (as sulphate) in the reaction vessel.

Di-*p*-chlorophenyl tetrasulphide (1 g.) in carbon tetrachloride (50 ml.) gave sulphur dioxide equiv. to 46·7 ml. of 0·2045N-alkali and *p*-chlorobenzenesulphonic anhydride equiv. to 22·3 ml. of 0·1952N-alkali (75%). In other experiments the anhydride was isolated as previously described.

Di*iso*propyl tetrasulphide (0·5 g.) gave sulphur dioxide and 1-methylethanesulphonic anhydride, respectively equiv. to 49·0 and 19·5 ml. (82%) of 0·1965N-alkali. The anhydride was not isolated.

Ozonolysis of Miscellaneous Sulphur Compounds.—*2 : 4-Dinitrobenzenesulphenic anhydride.* The product derived from the ozonolysis of the anhydride (0·272 g.), after evaporation of solvent, dissolved completely in water and required 6·5 ml. (100%) of 0·1965N-alkali for neutrality to screened methyl-red. Addition of *p*-toluidine hydrochloride (0·25 g.) in water (2 ml.) to the neutral solution reduced to small volume (2 ml.) gave *p*-toluidine 2 : 4-dinitrobenzenesulphonate, m. p. and mixed m. p. 244—245°.

Methyl benzenesulphenate. Ozonolysis of the sulphenate (2·0 g.) in carbon tetrachloride (50 ml.) ceased after an uptake of 0·7 mol. of ozone and gave an oil (2·3 g.); b. p. 55°/0·2 mm., n_D^{20} 1·5440 (Found: C, 53·8; H, 5·1; S, 20·0%; equiv., 155. Calc. for $C_7H_8O_2S$: C, 53·8; H, 5·1; S, 20·5%; equiv., 156). Alkaline hydrolysis gave sodium benzenesulphinate, as shown by the isolation of *S*-benzylthiuronium benzenesulphinate, m. p. and mixed m. p. 155·5—156°.

Thiophenol. The thiol (1 g.) was converted by ozone (1·6 mol.) into benzenesulphonic acid equiv. to 45·2 ml. (Calc., 44·5 ml.) of 0·2047N-alkali and characterised as the *S*-benzylthiuronium salt, m. p. and mixed m. p. 146—147°. In a further experiment the product left after the removal of solvent was treated in dry ether with an excess of aniline. No benzenesulphonanilide was detected, showing sulphonic anhydride to be absent: anilinium benzenesulphonate, m. p. and mixed m. p. 217—218°, was obtained in almost theoretical yield.

XUM

Phenyl benzenethiolsulphinate. Benzenesulphonic anhydride (85% yield by titration) and phenyl benzenethiolsulphonate (10%) were isolated from the products of ozonolysis as already described. *p*-Tolyl and *p*-chlorophenyl benzenethiolsulphinates also gave sulphonic anhydrides in 78 and 63% yield respectively, estimated by titration and by infrared spectroscopy, which also indicated thiolsulphonates (*ca.* 10%) to be formed in both cases.

Competitive Ozonolyses.—An equimolar mixture of oct-1-ene and di-*n*-butyl sulphide in carbon tetrachloride was treated with ozone equivalent to half of the octene. The olefin remaining and the solvent were distilled *in vacuo* from the products and by the comparison of the absorption (at 910 cm.$^{-1}$) of the distillate with a calibration curve from oct-1-ene it was found that the octene consumed was equivalent ($\pm$2%) to the ozone introduced, indicating a minimum rate factor between olefin and sulphide of 50 : 1.

Equimolar mixture of disulphides and thiolsulphinates with di-*n*-butyl sulphide were similarly ozonised to convert not more than half the sulphide into sulphoxide. On the assumption that, in the case of the disulphides and thiolsulphinates, the absorption of the first molecule of ozone constitutes the rate-determining step the rate of ozonolysis relative to that of monosulphide was calculated, approximately, from the ratio of the yields of acid (anhydride) produced in the presence and absence of monosulphide. Correction was made for the small amount of acidic products derived from the monosulphide.

Acknowledgment is made to Mr. G. M. C. Higgins and Mr. M. B. Evans for the spectroscopic data, and to Mr. P. W. Jones for experimental assistance. This work forms part of a programme of research undertaken by the Board of the British Rubber Producers' Research Association.

British Rubber Producers' Research Association,
48–56, Tewin Road, Welwyn Garden City, Herts. [*Received, June 28th*, 1957.]

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915. *Spectrophotometry in the Far Ultraviolet Region. Absorption Spectra of Some Amides and Cyclic Imides.*

By D. W. Turner.

The spectra of nine simple cyclic imides in the 1750—2000 Å region in aprotic solvents are described, together with those of related amides. The effect on intensity of progressive C_α-alkyl substitution is noted; a shift to longer wavelengths in glutarimide is ascribed to steric strain.

A double-beam spectrophotometer with photon counter for solution studies in the vacuum ultraviolet region is described.

Though some investigations have been made upon the far ultraviolet spectra of vapours of simple amides and their *N*-alkyl derivatives [1] and upon aqueous and ethanolic solutions of simple peptides,[2,3] no systematic quantitative examination of the spectra of more complex *C*-alkylated amides in aprotic solvents, or of cyclic imides, has been reported. An experimental difficulty lies in the low volatility and low solubility in aprotic solvents which must result from a high degree of intermolecular hydrogen bonding. Hydroxylic solvents, apart from having transmission limits not far below 1900 Å in a thin cell, are unsuitable when hydrogen bonding might directly affect the chromophore under consideration.

Many amides and imides are sufficiently soluble in aliphatic nitriles, and in hydrocarbon–nitrile mixtures, for spectroscopy. For the most polar compounds acetonitrile was used; it transmitted to 1800 Å ($E_{0\cdot02\text{cm.}} = 1\cdot0$) if carefully purified (see Experimental section). In other cases, however, specially purified *n*-hexane (cf. Potts [4]) containing

[1] Hunt and Simpson, *J. Amer. Chem. Soc.*, 1953, **75**, 4540.
[2] Ham and Platt, *J. Chem. Phys.*, 1952, **20**, 335.
[3] Saidel, *J. Amer. Chem. Soc.*, 1955, **77**, 3892.
[4] Potts, *J. Chem. Phys.*, 1952, **20**, 809.

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1—10% of propionitrile or valeronitrile had adequate solvent power and permitted measurements at 1740 Å ($E_{0\cdot02} = 1\cdot0$). No specific solvent effects were noticed; where solubility permitted, the same material was studied in more than one solvent mixture. The resultant spectra (see Fig. 1) were identical within experimental error.

All the succinimide derivatives have an absorption maximum at 51,300 cm.$^{-1}$ (1910 Å) independent of the nature or position of the substituents. The shift to longer wavelengths of 70 Å shown by glutarimide could be attributed to non-coplanarity of the imide group, in particular to a twist about the CO·NH bonds. The construction of models indicates that this twist may be as much as 40°, though the loss of resonance stabilisation which this would imply would probably result in the deformation's being partly taken up by C–C bonds of the ring. Since the twist increases the energy of the ground state relative to that of the excited state, the latter should involve an antibonding π orbital whose energy function has a minimum 90° from the planar configuration. This transition in the imides could thus be described as $N \longrightarrow V$, analogous to the longer-wavelength bands in formamide (1717 Å) and *NN*-dimethylformamide (1974 Å) vapours described by Hunt and Simpson.[1]

Peterson and Simpson [5] measured the direction of the transition-moment vector of the 1850 Å band of crystalline myristamide, finding alternative directions of either nearly parallel to the C–O bond or in the general direction of the C–N bond. If the above analogy is correct, sensitivity of the position of the 1910 Å imide band to twist about the C–N bond would favour the latter direction (also supported by theoretical calculations [5]). I hope to investigate further the quantitative effects of non-planarity on spectra in strained amides and imides.

The presence of alkyl substituents at C_α in both amides and imides results in a progressive decrease in intensity of the 1910 Å band (*ca.* 1750 Å in the amides) and in a series of similar symmetry (*e.g.*, **1**; **2**, **3**; **4**) the reduction is roughly proportional to the number of methyl groups introduced (a behaviour closely similar to that of the 1910 Å band in methyl ketones in the vapour state [6] and in hexane solution [7]). Comparison of the spectra of imides with amides having formally the same degree of C_α-substitution (numbers 2 or 3 with 11, 1 with 10 in Fig. 1) shows the $\epsilon_{max.}$ values to be in the ratio 2 : 1 within the limits of experimental error, as expected if the two halves of the imide group behave as independent amide chromophores.

Experimental

The Spectrophotometer.—A double-beam photoelectric vacuum instrument with fluorite optics was used, allowing greater precision in intensity measurements than usual in this region.

The double-beam section, inserted between the light source (a low-pressure, water-cooled hydrogen discharge operating at 0·2 A) and the entrance slit of a small prism spectroscope, contained a chopping wheel which interrupted each beam alternately 5 times per sec., and bore on its shaft a commutator. In the " sample " beam was placed the sample cell composed of two fluorite plates (0·5 in. diam.) separated by a 0·204 mm. brass spacer, in a brass surround, the seal being made on the edges of the plates by Araldite bonding resin. Entrance and exit ports entered the bottom and top of the cell tangentially in opposite directions. Oscillation of the flowing solution in the cell by means of an external pump produced vigorous stirring, thus, preventing the formation of stagnant regions in the cell in which products of photolysis otherwise accumulated.

In the " reference " beam, the cell was replaced by an accurately adjustable slit by which the cell absorption could be balanced. The recombined beams, after dispersion by a conventional 60° prism spectrograph, passed through an exit slit (0·002 in., equivalent to ~100 cm.$^{-1}$) behind which was a photon counter; the whole assembly of slit, counter, and associated head amplifier could be moved along the focal plane by a lead screw operated by a servo-motor. Impulses from the counter, after amplification ($\times$ *ca.* 2 $\times$ 10^4) and shaping (to square pulses,

[5] Peterson and Simpson, *J. Amer. Chem. Soc.*, 1955, **77**, 3929.
[6] Duncan, *J. Chem. Phys.*, 1940, **8**, 444.
[7] Turner, unpublished work.

duration 20 μsec.), were divided into two channels (corresponding to sample and reference beams) by the chopping wheel commutator, and fed to conventional diode rate-meter circuits. The ratio of the potentials developed was recorded continuously on paper scaled in optical density. Linearity between rate-meter output and count-rate was checked with a high-speed scaler, and circuit parameters were adjusted to allow a maximum deviation from linearity of 2%. At the count-rates used (~1000 counts/sec.) an integrating time constant of 2 sec. gave deviations of E from the mean of 5%. Graphical interpolation on the chart enabled the

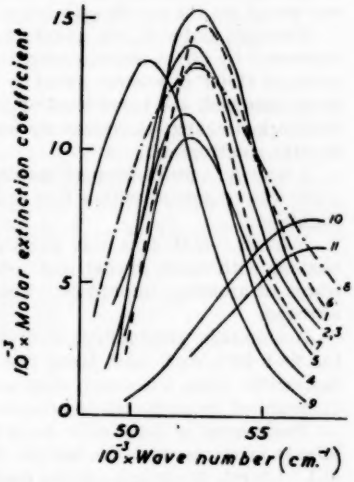
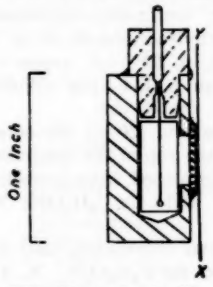


FIG. 1.

Compound, with solvent in parentheses.—1, Succinimide (A, E); 2, (±)-dimethylsuccinimide (A); 3, *meso*-dimethylsuccinimide (A); 4, tetramethylsuccinimide (F); 5, *cis*-hexahydrophthalimide (F); 6, *gem.*-dimethylsuccinimide (D); 7, methylsuccinimide (F); 8, *cyclo*hexyl*spirocyclo*propylsuccinimide (C, D); 9, glutarimide (A); 10, propionamide (F); 11, *iso*butyramide (A, F).

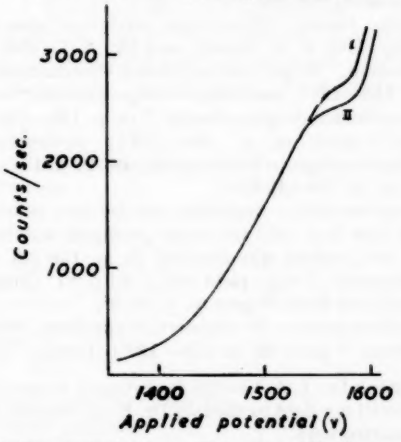
Solvents.—A, Acetonitrile; B, *n*-hexane (90%)–valeronitrile (10%); C, *n*-hexane (95%)–valeronitrile (5%); D, *n*-hexane (99%)–valeronitrile (1%); E, *n*-hexane (95%)–propionitrile (5%); F, *n*-hexane (98%)–propionitrile (2%).

FIG. 2. *The photon counter.*



XY, Plane of exit slit.

FIG. 3. *Counter operating characteristic.*



Scaler paralysis time: (I) 5 μsec.; (II) 50 μsec.

error to be reduced to at most ±2%. The solvent absorption curve was recorded frequently, generally immediately after that of each sample.

The Photon Counter.—This was constructed of brass (Fig. 2) with a copper iodide [8,9] (on copper foil) photoemissive surface, and had a 0·003 in. tungsten wire anode. It was filled with methane, and operated as a proportional counter at 1560 v (Fig. 3).

[8] Lormean, *Compt. rend.*, 1947, **225**, 453, 865; 1948, **227**, 274.
[9] Turner, *Nature*, in the press.

The photoemissive surface was prepared by treatment of the cleaned and degreased copper foil cylinder with a dilute solution of iodine in carbon tetrachloride until a visible film of iodide had formed; the treated foil was then thoroughly washed with carbon tetrachloride and dried at room temperature before insertion in the counter. After assembly, the counter was evacuated to 10^{-4} mm. for 2 hr., flushed with pure methane, filled to 10 cm. pressure, and sealed.

Sensitivity.—A larger (0·5 in. diam.) experimental counter with a magnetically movable photocathode allowed the photosensitivity of this surface to be compared with that of clean copper (photoelectric yield at 2000 Å *ca.* 10^{-4}) under the same conditions. A ratio of $<10^3 : 1$ was found for the wavelength range 2300 Å (photothreshold)—1850 Å (air cut-off).

The high order of the quantum efficiency of the copper iodide surface in this region was confirmed by direct measurement by use of an electrically heated platinium strip whose temperature (1500° c) was measured by an optical pyrometer. Conditions of black-body radiation being assumed, the lower level of quantum efficiency was 10^{-2} count per incident quantum. No marked change in sensitivity was apparent between 1900 Å and 1450 Å, the limit of the fluorite spectrograph.

Linearity.—Strict proportionality between count rate and light intensity over a range of $<10^3$ was confirmed with a fast scaler (paralysis time, 3 μsec.) for count rates up to 20,000 counts/sec.

Solvents.—*n*-Hexane was purified [4] by treatment with chlorosulphuric acid followed by washing with water, drying, and distillation from sodium. Activated silica gel finally removed traces of aromatic impurities. The pure solvent was stored over freshly cut sodium under nitrogen.

Acetonitrile, propionitrile, and valeronitrile were repeatedly distilled from phosphoric oxide, the first 10% each time being rejected. For acetonitrile, which was used undiluted (being immiscible with *n*-hexane), five such distillations were required before absorption by an unidentified impurity fell to acceptable levels (*i.e.*, $E_{0.02} > 0{\cdot}3$ at 1900 Å).

Preparation of Solutions.—Since the materials studied were all only slightly soluble in the solvent mixtures used, the sample (2—4 mg. ±0·02 mg.) was dissolved initially in the nitrile (0·1—1·0 ml. depending on the final solvent proportion desired), and diluted with *n*-hexane to 10 ml., the mixture being stirred by a stream of nitrogen bubbles to remove all oxygen before admission to the cell.

Cyclic Imides.—These were analytical samples presented by Dr. J. A. Elvidge, Dr. M. Whalley, Miss P. M. Brown, and Mr. A. L. Bull (who are thanked), and used without further purification. M. p.s were as follows: Succinimide, m. p. 125—126°; (±)-dimethylsuccinimide,[9a] m. p. 125—127°; *meso*-dimethylsuccinimide,[9a] m. p. 45—47°; tetramethylsuccinimide, m. p. 87°; *cis*-hexahydrophthalimide,[10] m. p. 136—137°; *gem.*-dimethylsuccinimide, m. p. 105—106° (Sircar [11] gives m. p. 105—106°); methylsuccinimide, m. p. 62° (cf. Arppe [12]); *cyclo*hexyl*spirocyclo*propylsuccinimide, m. p. 161°; glutarimide, m. p. 154—155° (Wolffenstein [13] gives m. p. 154—155°).

Propionamide.—Ammonia was led into refluxing propionic acid (20 g.) (air condenser) at such a rate that only the water produced was removed from the top of the condenser. After 4 hr. the product was distilled (b. p. 150°/20 mm.) and crystallised from benzene to yield propionamide (7·8 g., yield 40%), m. p. 81° (Found: N, 19·0. Calc. for C_3H_7ON: N, 19·2%). Mitchell and Reid [14] give m. p. 81·3°.

iso*Butyramide.*—A commercial specimen, recrystallised from chloroform, had m. p. 129° (Hofmann [15] gives m. p. 128—129°) (Found: N, 15·96. Calc. for $C_4H_9O_2N$: N, 16·08%).

I thank Dr. J. A. Elvidge for bringing to my attention the lack of ultraviolet data for imides, and record my debt to the late Dr. E. A. Braude, at whose instance far ultraviolet investigations were started here.

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[*Received, May 10th,* 1957.]

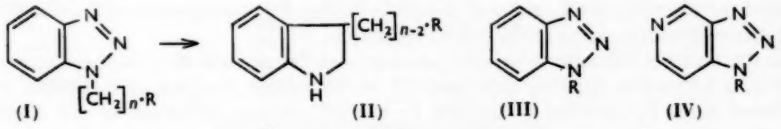
[9a] Linstead and Whalley, *J.*, 1954, 3722.
[10] Ficken, France, and Linstead, *J.*, 1954, 3730.
[11] Sircar, *J.*, 1927, 1255.
[12] Arppe, *Annalen*, 1853, **87**, 230.
[13] Wolffenstein, *Ber.*, 1892, **25**, 2777.
[14] Mitchell and Reid, *J. Amer. Chem. Soc.*, 1931, **53**, 1881.
[15] Hoffmann, *Ber.*, 1882, **15**, 982.

916. *The Graebe–Ullmann Carbazole Synthesis.*

By B. W. Ashton and H. Suschitzky.

Some benzo- (III) and pyridino(3′ : 4′-4 : 5)-1 : 2 : 3-triazoles (IV) with 1-alkyl, 1-alkylaryl and 1-*cyclo*hexyl substituents have been pyrolysed to see whether the Graebe–Ullmann carbazole synthesis could be extended to intramolecular arylation of alkyl CH groups. These thermal decompositions generally lead to secondary amines. The preparative value of this synthesis is, therefore, limited to triazoles with 1-aromatic or 1-heteroaromatic substituents.

The Graebe–Ullmann synthesis has been successfully applied to the preparation of carbazoles [1] and carbolines,[2] but the thermal decomposition of benzo- (III) or pyridino-(3′ : 4′-4 : 5)-1 : 2 : 3-triazoles (IV) with 1-alkyl, 1-alkylaryl, or 1-*cyclo*alkyl substituents has not been reported. We have now sought to extend this synthesis to such compounds which by analogy were expected to lose nitrogen when heated and to cyclise by arylation of an alkyl CH group. This extension could provide a route (I) ⟶ (II) to 3-substituted indolines (II).



(I) (II) (III) (IV)

For the preparation of triazoles *o*-chloronitrobenzene or 4-chloro-3-nitropyridine was condensed with the requisite amine, the nitro-compound obtained being reduced with sodium dithionite to a diamine which was then treated with nitrous acid. Pyrolyses were usually carried out in sealed tubes, as most triazoles proved very stable when heated in a liquid medium such as syrupy phosphoric acid, liquid paraffin, or "Silicone Oil." A small amount of inflammable gas, together with ammonia, was generally noticed on opening the tubes, and liquid hydrocarbons could often be separated from the mixture. Nitrogen-containing products were usually identified as picrates. The results of the decompositions are summarised in Table 1.

Table 1.

Substituent	Products	Yield (%)
1-Substituted benzo-1 : 2 : 3-triazoles		
H	Aniline	40
*cyclo*Hexyl	Diphenylamine	5
	Carbazole	15
Benzyl	*N*-Benzylaniline	4
	Phenanthridine	4
Phenethyl	*N*-Phenethylaniline	7
Butyl	*N*-Butylaniline	18
Allyl	*N*-Allylaniline	14
	Aniline	5
	Quinoline	5
1-Substituted pyridino(3′ : 4′-4 : 5)-1 : 2 : 3-triazoles		
*cyclo*Hexyl	4-*cyclo*Hexylaminopyridine	6
Benzyl	4-Benzylaminopyridine	8
Phenethyl	4-Aminopyridine	6
1 : 1′-Substituted benzobis-1 : 2 : 3-triazole		
Hexamethylene	Aniline	10

We isolated phenanthridine from the decomposition products of 1-benzylbenzo-1 : 2 : 3-triazole (III; R = Ph·CH_2), as reported by Gibson,[3] and also some *N*-benzylaniline.

[1] Ullmann, *Annalen*, 1904, **332**, 82; Coker, Plant, and Turner, *J.*, 1951, 111.
[2] Späth and Eiter, *Ber.*, 1940, **73**, 719; Bremer, *Annalen*, 1934, **514**, 279.
[3] Gibson, *J.*, 1956, 1076.

Benzylpyridino(3′ : 4′-4 : 5)-1 : 2 : 3-triazole (IV; R = Ph·CH_2), however, did not cyclise and gave only 4-benzylaminopyridine.

Small amounts of carbazole and diphenylamine were obtained on pyrolysis of 1-*cyclo*hexylbenzo-1 : 2 : 3-triazole (III; R = C_6H_{11}). The formation of carbazole, however, is probably not caused by ring closure of Graebe–Ullmann type between the aromatic nucleus and *cyclo*hexane (followed by dehydrogenation), because we found that *N-cyclo*hexylaniline under similar conditions also gives a mixture of the two amines. The primary reaction product is probably *N-cyclo*hexylaniline, yielding by dehydrogenation diphenylamine which is known to cyclise to carbazole when strongly heated.[4] In some decompositions loss of nitrogen and dealkylation occurred.

From the pyrolysis products of 1-allylbenzo-1 : 2 : 3-triazole small quantities of quinoline and *N*-allylaniline were isolated. Since, however, one of the compounds produced by a sealed-tube reaction with *N*-allylaniline [5] is quinoline, its presence is probably not accounted for by the Graebe–Ullmann reaction.

Apart from the triazoles listed above, 5-chloro- and 5-methyl-1-2′-pyridylbenzo-1 : 2 : 3-triazole were heated in syrupy phosphoric acid and gave in good yield the corresponding α-carbolines needed for another research. In an unsuccessful attempt to improve the overall yield of α-carboline previously made by a Graebe–Ullmann synthesis,[6] we prepared the intermediate 2-amino-*N*-2′-pyridylaniline by condensation of 2-aminopyridine and 1-chloro-2-nitrobenzene, followed by reduction.

As the Graebe–Ullmann synthesis has a superficial resemblance to the Pschorr type reaction, a suggestion by Hey and Mulley,[7] which relates the ease of formation of five-membered rings by internal cyclisation to the internuclear distances in the unstrained molecules, was applied to our problem. From an inspection of Courtauld models and from calculations based on diagrams, the distances between the relevant aryl- and alkyl-carbon atoms in our structures are found to be 2·0 Å. Since this value is close to that found for molecules undergoing Graebe–Ullmann reactions, the distance involved in these cyclisations cannot be regarded as decisive for the success of the reaction. Some correlation can, however, be made between the nature of substituents in the benzene ring of benzo-1 : 2 : 3-triazoles and yields obtained on pyrolysis. Electron-supplying substituents lead to generally good results,[8,9] whereas electron-withdrawing groups (including halogens) lead to negligible yields.[9,10] On this basis the mechanism of the Graebe–Ullmann reaction appears to be ionic and the failure of benzo- or pyridino-1 : 2 : 3-triazoles with 1-alkyl substituents to cyclise may be explained by the inertness of inactivated alkyl structures towards heterolytic substitution.

TABLE 2. *Ultraviolet absorption maxima* ($m\mu$) *in* EtOH.

Substituent	λ_1	ε_1	λ_2	ε_2	λ_3	ε_3
1-Substituted benzo-1 : 2 : 3-triazoles						
H	250	6560	255	6449	270	5260
*cyclo*Hexyl	254	6880	259	6940	275	4690
Benzyl	253	6490	259	6410	275	4170
Phenethyl	254	6770	259	6685	277	4510
1-Substituted pyridino(3′ : 4′-4 : 5)-1 : 2 : 3-triazoles						
*cyclo*Hexyl	261	5415	—	—	—	—
Benzyl	261	5725	—	—	—	—
Phenethyl	257	6050	—	—	—	—

Absorption spectra of a number of triazoles are given in Table 2. The curves of 1-benzyl- and 1-phenethyl-substituted benzo- and pyridino-triazoles hardly differ from

[4] Graebe, *Ber.*, 1872, **5**, 377.
[5] Carnahan and Hurd, *J. Amer. Chem. Soc.*, 1930, **52**, 4586.
[6] Lawson, Perkin, and Robinson, *J.*, 1924, 626.
[7] Hey and Mulley, *J.*, 1952, 2276.
[8] Allen, *Chem. Listy*, 1954, **48**, 1075.
[9] Preston, Tucker, and Cameron, *J.*, 1942, 500.
[10] Allen and Suschitzky, *J.*, 1953, 3845.

those of their respective 1-*cyclo*hexyl derivatives, undoubtedly owing to the presence of the CH_2 and $CH_2{\cdot}CH_2$ groups whose insulating effects prevent conjugation of the benzene ring with the triazole systems.

Experimental

Condensations.—(*a*) *o*-Chloronitrobenzene (1 mol.) and the appropriate amine (2·5 mol.) were heated for 5—10 hr. on a water-bath. The resulting oil was extracted with water and then with concentrated hydrochloric acid. Basification of the acid extract with aqueous ammonia was followed by recrystallisation of the nitro-amine from ethanol.

(*b*) To a 10% solution of the amine (2·5 mol.) in benzene was slowly added a similar solution of 4-chloro-3-nitropyridine [11] (1 mol.) and the mixture refluxed for 5 hr. The precipitated amine hydrochloride was filtered off and a crude product was obtained by removing the solvent from the filtrate by distillation. Recrystallisation occurred from ethanol. The compounds thus prepared are recorded in Table 3.

Table 3.

N-Substituted o-nitroanilines

		Found (%)				Required (%)			
Substituent	M. p.	C	H	N	Formula	C	H	N	Yield (%)
*cyclo*Hexyl	105°	65·5	7·3	13·0	$C_{12}H_{16}O_2N_2$	65·5	7·3	12·7	87
Benzyl	75 [a]	—	—	—	—	—	—	—	80
Phenethyl	72	69·2	5·6	11·9	$C_{14}H_{14}O_2N_2$	69·4	5·8	11·6	75
Butyl	[b]	62·0	7·6	14·1	$C_{10}H_{14}O_2N_2$	61·8	7·2	14·4	70
Allyl	[c]	60·3	5·8	16·0	$C_9H_{10}O_2N_2$	60·7	5·6	15·7	54
2′-Pyridyl	66—67	61·8	4·2	19·9	$C_{11}H_9O_2N_3$	61·4	4·2	19·5	9
4-Chloro-2′-pyridyl	108	53·2	3·4	17·1	$C_{11}H_8O_2N_3Cl$	52·9	3·2	16·9	10
4-Methyl-2′-pyridyl	97	62·9	4·8	—	$C_{12}H_{11}O_2N_3$	62·9	4·8	—	9
4-N-Substituted 4-amino-3-nitropyridine									
*cyclo*Hexyl	102—103	60·0	6·8	18·7	$C_{11}H_{15}O_2N_3$	59·7	6·8	19·0	90
Benzyl	100—101	63·1	4·9	18·0	$C_{12}H_{11}O_2N_3$	62·9	4·8	18·3	70
Phenethyl	83	63·8	5·4	17·1	$C_{13}H_{13}O_2N_3$	64·2	5·3	17·3	78
o-Ethoxyphenyl	100	59·8	5·0	15·8	$C_{13}H_{13}O_3N_3$	60·3	5·0	16·2	86
Di-*o*-nitroanilinohexane	110	60·4	5·9	16·0	$C_{18}H_{22}O_4N_4$	60·3	6·1	15·6	48

[a] Gibson, *J.*, 1956, 1076, gives m. p. 74—75°. [b] B. p. 161°/8 mm. [c] B. p. 260°/76 mm.

Reductions.—To a boiling 5—10% ethanolic solution of the nitro-compound (1 mol.) 40% aqueous potassium hydroxide (10 mol.) was added, followed slowly by a saturated solution of sodium dithionite until the mixture became colourless or straw-yellow. After distillation of ethanol the mixture was poured into water. The precipitated amine was purified from water or ethanol. *N*-Allyl-*o*-nitroaniline gave some unidentified products by this method, but when reduced with stannous chloride and hydrochloric acid, yielded *N*-allyl-2-aminoaniline as a

Table 4.

N-Substituted o-aminoanilines

		Found (%)				Required (%)			
Substituent	M. p.	C	H	N	Formula	C	H	N	Yield (%)
*cyclo*Hexyl	51°	75·8	10·0	14·4	$C_{12}H_{18}N_2$	75·8	9·5	14·7	91
Benzyl	78	78·8	7·2	14·4	$C_{13}H_{14}N_2$	78·8	7·0	14·1	74
Phenethyl	55	79·4	7·5	12·9	$C_{14}H_{16}N_2$	79·2	7·5	13·2	66
Butyl	35	73·3	9·8	16·9	$C_{10}H_{16}N_2$	73·2	9·8	17·1	62
Allyl	[a]	72·8	8·0	19·2	$C_9H_{12}N_2$	72·9	8·1	18·9	45
4-N-Substituted 3 : 4-diaminopyridines									
*cyclo*Hexyl	143	68·9	8·8	22·2	$C_{11}H_{17}N_3$	69·1	8·9	21·9	40
Benzyl	119	72·1	6·6	21·0	$C_{12}H_{13}N_3$	72·4	6·5	21·1	84
o-Ethoxyphenyl	232	67·7	7·0	18·0	$C_{13}H_{15}ON_3$	68·1	6·6	18·2	54
Di-*o*-aminoanilinohexane	121	72·6	9·0	19·0	$C_{18}H_{26}N_4$	72·5	8·7	18·8	64

[a] B. p. 120°/10 mm.

light-sensitive, unstable oil, whose *benzoate* had m. p. 140° (Found: C, 76·4; H, 6·6. $C_{16}H_{16}ON_2$ requires C, 76·2; H, 6·3%). 3-Amino-4-phenethylaminopyridine was too unstable for analysis and had to be used immediately for triazole formation. *Compounds* thus prepared are listed in Table 4.

[11] Kruger and Mann, *J.*, 1955, 2758.

Triazole Formation.—A cooled solution (2—5%) of the diamine in 2N-hydrochloric acid to which a few ml. of ethanol had been added was diazotised at 0—5° with 5% aqueous sodium nitrite, stirring being continued for 1 hr. The mixture, after addition of a few ml. of concentrated hydrochloric acid to dissolve precipitated triazole, was boiled (charcoal), filtered and basified with ammonia (*d* 0·88). The triazole was filtered off and recrystallised from water, aqueous ethanol, or acetone. The triazoles obtained in this way are collected in Table 5.

Pyrolysis of Triazoles.—(a) *In syrupy phosphoric acid.* A solution of the triazole (0·5 g.) in syrupy phosphoric acid (2 ml.) was heated at 200° until evolution of nitrogen had ceased. This was determined by comparison with a blank experiment. The product was obtained by extracting the basified (sodium hydroxide) mixture with ether. 5-Chloro-1-2′-pyridylbenzo-1 : 2 : 3-triazole gave 6-*chloro-α-carboline* (37%), m. p. 229—230° (Found: C, 65·1; H, 3·6; N, 14·1; Cl, 17·7. $C_{11}H_7N_2$ requires C, 65·2; H, 3·5; N, 13·8; Cl, 17·5%). Under similar conditions 5-methyl-1-2′-pyridylbenzo-1 : 2 : 3-triazole yielded 6-*methyl-α-carboline* (46%), m. p. 220—221° (Found: C, 79·1; H, 5·7. $C_{12}H_{10}N_2$ requires C, 79·1; H, 5·5%).

TABLE 5.

Substituent	M. p.	Found (%) C	H	N	Formula	Required (%) C	H	N	Yield (%)
1-*Substituted benzo*-1 : 2 : 3-*triazoles*									
*cyclo*Hexyl	104°	71·6	7·7	21·2	$C_{12}H_{15}N_3$	71·6	7·5	20·9	66·5
Benzyl	115 [a]	—	—	—	—	—	—	—	35
Phenethyl	37	75·0	5·7	18·6	$C_{14}H_{13}N_3$	75·3	5·8	18·8	52
Butyl	[b]	68·7	7·2	24·0	$C_{10}H_{12}N_3$	68·6	7·4	24·0	56
Allyl	[c]	67·9	5·8	26·6	$C_9H_9N_3$	67·9	5·7	26·4	37
1-*Substituted pyridino*(3′ : 4′-4 : 5)-1 : 2 : 3-*triazoles*									
*cyclo*Hexyl	97	65·6	6·8	27·6	$C_{11}H_{14}N_4$	65·3	6·9	27·7	69
Benzyl	120 [d]	—	—	—	—	—	—	—	85
Phenethyl	83	69·4	5·3	25·1	$C_{13}H_{12}N_4$	69·6	5·4	25·0	90
o-Ethoxyphenyl	85	64·9	6·2	23·0	$C_{13}H_{13}ON_4$	65·0	5·0	23·3	72
1 : 1′-*Substituted bisbenzo*-1 : 2 : 3-*triazole*									
Hexamethylene	107	67·2	6·4	26·6	$C_{18}H_{20}N_8$	67·5	6·3	26·3	54
5-*Substituted* 1-2′-*pyridylbenzo*-1 : 2 : 3-*triazoles*									
5-Methyl	109	68·4	4·7	27·0	$C_{12}H_{10}N_4$	68·5	4·7	26·7	63
5-Chloro	152	57·2	3·0	24·6	$C_{11}H_7N_4Cl$	57·3	3·0	24·3	90·7

[a] Gibson [3] gives m. p. 115—116°. [b] B. p. 176°/18 mm. [c] B. p. 160°/16 mm. [d] Bremer (*Annalen*, 1935, **518**, 274) records m. p. 124°.

(b) *In a sealed tube.* The triazole (0·5—0·8 g.) was heated in a sealed Pyrex tube (2″ × ⅜″) at 400° for 0·75 hr. In order to avoid losses due to the ensuing explosion the glass tube was opened by dropping it down a copper tube. Extraction of the mixture (Soxhlet) with light petroleum (b. p. 60—80°) gave usually, after evaporation of the solvent, a syrup. Nitrogenous constituents were extracted from the syrup with hydrochloric acid, the extract basified, and the residue chromatographed on alumina with benzene. From the pyrolysis products of 1-*cyclo*hexylbenzo-1 : 2 : 3-triazole, carbazole was not removed by extraction with hydrochloric acid and thus was separable from diphenylamine. Products were identified by analysis, their picrates, and mixed m. p. determinations. The results of these decompositions are collected in Table 1.

4-cyclo*Hexylaminopyridine.*—4-Chloropyridine (7 g.), *cyclo*hexylamine (15 g.), and anhydrous potassium carbonate (2 g.) were refluxed for 15 hr. Distillation of the filtered mixture gave a colourless liquid (b. p. 70—80°/75 mm.) which on sublimation at 2 mm. yielded 4-cyclo*hexylaminopyridine*, m. p. 140° (10%) (Found: C, 74·9; H, 9·0. $C_{11}H_{16}N_2$ requires C, 75·0; H, 9·1%).

4-*Phenethylaminopyridine.*—By the above procedure 4-chloropyridine and phenethylamine gave 4-*phenethylaminopyridine*, m. p. 108—109° (10%) (Found: C, 78·9; H, 6·8. $C_{13}H_{14}N_2$ requires C, 78·8; H, 7·1%).

Grateful acknowledgment is made to the Directors of Boots Pure Drug Co., Nottingham, for a Research Studentship (to B. W. A.). We thank Dr. D. A. Peak for his interest and therapeutic tests, and Dr. C. E. Seaman for discussion.

ROYAL TECHNICAL COLLEGE, SALFORD, LANCS. [*Received, June 4th*, 1957.]

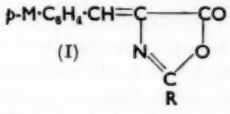
917. *Cyto-active Amino-acids and Peptides. Part IV.*[1] *Synthesis of α-[p-Di-(2-chloroethyl)amino-benzylidene- and -benzyl-]hippuramides and -hippuramido-acids.*

By F. Bergel and J. A. Stock.

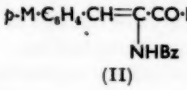
4-[*p*-Di-(2-chloroethyl)aminobenzylidene]-2-phenyloxazol-5-one [I; R = Ph; M = $(Cl\cdot CH_2\cdot CH_2)_2N$] is described. This compound, when treated with ammonia, primary amines, α-amino-acids, or α-amino-acid esters, gave " nitrogen mustard "-substituted unsaturated amides and peptides (as II and III) which were reduced to the corresponding substituted phenylalanine derivatives (as IV and V). An analogous thiazolone has also been prepared.

Syntheses of " nitrogen-mustard " analogues of L-, D-, and DL-tyrosine and of DL-thyronine were described in previous parts of this series,[1] which dealt with potential anti-tumour agents of an α-amino-acid character. We now report an extension of this work aiming at the preparation of related dipeptides.

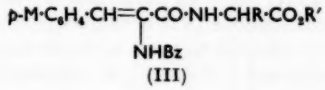
Although known to be of limited value, Bergmann's azlactone synthesis [2] was employed because of the ready availability of *p*-di-(2-chloroethyl)aminobenzaldehyde.[3] When the latter was heated with hippuric acid in acetic anhydride in the presence of sodium acetate, the azlactone [I; R = Ph, M (in this and all following formulæ) = $(Cl\cdot CH_2\cdot CH_2)_2N$] was obtained in yields of 60% or more. This reacted readily with ammonia and primary amines to give α-[*p*-di-(2-chloroethyl)aminobenzylidene]hippuramides (II), and with amino-



(I)



(II)



(III)

acids and their esters to give the corresponding hippuramido-acids and -esters (III). These compounds may be considered as dehydro-derivatives of N^{α}-benzoylphenylalanine amides and peptides. In order to achieve satisfactory reactions three or more molar equivalents of the amine or amino-acid derivative had to be used. The crystalline compounds prepared in this way are listed in Table 1. They comprise derivatives of ammonia (II; R = H), ethylamine (II; R = Et), and *cyclo*hexylamine (II; $R = C_6H_{11}$); of glycine (III; R = R′ = H), DL- and L-alanine (III; R = Me, R′ = H), and L-valine (III; $R = Me_2CH$, R′ = H); and of the ethyl esters of glycine (III; R = H, R′ = Et), L-leucine (III; $R = Me_2CH\cdot CH_2$, R′ = Et), and DL-phenylalanine (III; $R = Ph\cdot CH_2$, R′ = Et). The azlactone (I; R = Ph) reacted with L-leucine, L-tyrosine ethyl ester, DL-aspartic acid, L-histidine, L-cysteine, and DL-methionine but the products resisted crystallisation. Aniline and *p*-aminobenzoic acid did not react with the azlactone (I; R = Ph) under the conditions outlined in the Experimental section, the azlactone being recovered unchanged.

Conversion of compounds of type (II) and (III) into DL-phenylalanine derivatives (IV) and (V) was first attempted by catalytic hydrogenation. This reduction of the glycine (III; R = R′ = H) and of the DL-alanine derivative (III; R = Me, R′ = H) could be achieved only by using a mixture of Adams platinum oxide, palladium–charcoal, and Raney nickel. Any one or any pair of these catalysts was ineffective. However, it was found that the *cyclo*hexylamide (II; $R = C_6H_{11}$) could be hydrogenated over Raney nickel. Three other compounds were reduced, not always readily, with the three-catalyst mixture, namely, the derivatives of ammonia (II; R = H), L-alanine (III; R = Me, R′ = H), and DL-phenylalanine ethyl ester (III; $R = Ph\cdot CH_2$, R′ = Et).

[1] Part I, Bergel and Stock, *J.*, 1954, 2409; Part II, Bergel, Burnop, and Stock, *J.*, 1955, 1223; Part III, Bergel and Lewis, *J.*, 1957, 1816.
[2] Carter, " Organic Reactions," Wiley, New York, 1946, Vol. III, p. 198.
[3] Anker and Cook, *J.*, 1944, 489.

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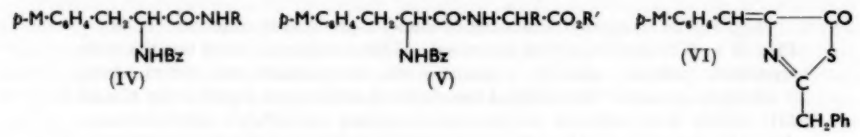
While zinc in glacial acetic acid was not effective, the addition of concentrated hydrochloric acid to this system led to very rapid and efficient reduction, yields being substantially higher than by catalytic hydrogenation (Table 2). The apparent lack of optical activity in the reduced L-alanine and L-leucine ethyl ester derivatives (Table 2; Nos. 6 and 7), the former prepared by either method of reduction, does not indicate that



racemisation had occurred. After hydrolysis of the compounds with 6N-hydrochloric acid, the solutions showed rotations comparable with those to be expected from the presence of an equivalent concentration of L-alanine and L-leucine respectively. Moreover, the m. p. of the L-alanine derivative (Table 2, No. 6) was about 25° lower than that of the corresponding DL-alanine peptide (No. 5).

The methods outlined above thus enabled us to prepare several N^{α}-benzoyl-dipeptides carrying a " nitrogen mustard " group on the phenylalanine moiety. The benzoyl group does not, however, lend itself to removal by means which would preserve the peptide link. We therefore sought to vary the azlactone so as to have ultimately an easily removable *N*-acyl group. To this end we attempted to prepare the azlactones (I; R = Me), (I; R = CF_3), (I; R = Ph·CH_2), and (I; R = Ph·CH_2·O) but failed. We did, however, synthesise the thiazolone (VI) from phenyl(thioacetyl)glycine but this did not give crystalline products when allowed to react with ethylamine or *cyclo*hexylamine. This approach was therefore postponed. However, as indicated in a preliminary communication,[4] we are investigating the use of the readily removable *o*-cyanobenzoyl group in the preparation of peptides related to the compounds described in this paper but possessing a free amino-group. That such an amino-group may be required for powerful anti-tumour activity is illustrated by the apparent ineffectiveness [5] on the Walker carcinoma 256 of the azlactone (I; R = Ph), the thiazolone (VI), of the dehydro-compounds as given on Table 1, and of the glycine peptide (V; R = R′ = H). While none of these compounds has been tested yet up to the limit of tolerance, it seems that pronounced anti-tumour action in this series may depend on the presence of zwitterion systems.

Experimental

4-[p-*Di*-(2-*chloroethyl*)*aminobenzylidene*]-2-*phenyloxazol*-5-*one* (I; R = Ph) (cf. Buck and Ide [6]).—*p*-Di-(2-chloroethyl)aminobenzaldehyde [3] (4·92 g.), hippuric acid (3·58 g., 1·0 mol.), powdered anhydrous sodium acetate (1·64 g., 1·0 mol.), and acetic anhydride (6 ml.) were heated with stirring at about 120°. Complete dissolution occurred within a few minutes. The red solution was then heated on a steam-bath for about 25 min. It deposited red crystals on cooling. Water (7 ml.) was added to the cold mixture. The aqueous layer was poured off after about 15 min., and the solid residue washed with water, collected, and dried. The *oxazolone* crystallised from benzene in bright red prisms (4·89 g., 63%), m. p. 132—135° (with previous softening, and clarification at 142°). Omission of sodium acetate from the reaction mixture resulted in a slightly lower yield. Recrystallisation from benzene raised the m. p. to 135—138° (softening from 122°; clarification and meniscus 142—145°) (Found: C, 64·0; H, 5·0; N, 7·0; Cl, 16·5. $C_{20}H_{18}O_2N_2Cl_2,\frac{1}{2}C_6H_6$ requires C, 64·5; H, 4·9; N, 6·5; Cl, 16·6%). Crystallisation from Cellosolve gave light tan solvent-free prisms of much sharper m. p. (141—142°) (Found: C, 61·5; H, 4·7; N, 7·4; Cl, 18·0. $C_{20}H_{18}O_2N_2Cl_2$ requires C, 61·7; H, 4·6; N,

[4] Bergel and Stock, *Proc. Chem. Soc.*, 1957, 60.
[5] Personal communication from Professor A. Haddow.
[6] Buck and Ide, *Org. Synth.*, Coll. Vol. II, 1943, p. 55.

TABLE 1.

No.	Compound	Isomer	Cryst. from	M. p.	$[\alpha]_D$	Yield (%)	Formula	Found (%) C	H	N	Cl	Required (%) C	H	N	Cl
1	II; R = H	—	A [a]	179—180°	—	95	$C_{20}H_{21}O_2N_3Cl_2$	58·9	5·25	—	17·2	58·9	5·25	—	17·5
2	II; R = Et	—	B [a]	165—166	—	76	$C_{22}H_{25}O_2N_3Cl_2$	—	—	9·25	16·25	—	—	9·7	16·4
3	II; R = *cyclo*hexyl	—	C [b]	177—178	—	75	$C_{26}H_{31}O_2N_3Cl_2$	63·75	6·6	8·3	14·4	63·95	6·35	8·6	14·55
4	III; R = R′ = H	—	B [c]	190—191	—	74	$C_{22}H_{23}O_4N_3Cl_2$	—	—	8·9	14·8	—	—	9·05	15·3
5	III; R = Me; R′ = H	DL	D [a]	176—178	—	81	$C_{23}H_{25}O_4N_3Cl_2$	57·8	5·3	8·4	14·7	57·75	5·2	8·8	14·9
6	III; R = Me; R′ = H	L	E [a]	167—169	+31° ± 1° [d]	82	,,	57·2	5·2	8·3	14·75	57·75	5·2	8·8	14·9
7	III; R = Me_2CH; R′ = H	L	D [c]	166—167	−15 ± 1·5° [e]	79	$C_{25}H_{29}O_4N_3Cl_2$	59·2	5·9	8·0	14·6	59·3	5·7	8·3	14·0
8	III; R = H; R′ = Et	—	F [a]	143—144	—	80	$C_{24}H_{27}O_4N_3Cl_2$	58·8	5·7	8·3	14·4	58·5	5·5	8·5	14·4
9	III; R = Me_2CHCH_2; R′ = Et	L	A [a]	177—178	+20 ± 2° [f]	73 [g]	$C_{28}H_{35}O_4N_3Cl_2$	61·25	6·05	7·9	13·3	61·3	6·4	7·7	13·0
10	III; R = $PhCH_2$; R′ = Et	DL	E [ah]	141—142	—	60	$C_{31}H_{29}O_4N_3Cl_2$	64·0	5·6	7·3	12·15	63·9	5·7	7·2	12·2

A, Aqueous ethanol. B, Methanol. C, Ethanol. D, Aqueous Cellosolve. E, Aqueous propan-1-ol. F, Pentanol. [a] Yellow rods or needles. [b] Colourless needles. [c] Yellow prisms. [d] *c* 1·54 in dioxan at 25°. [e] *c* 0·29 in EtOH at 25°. [f] *c* 1·1 in dioxan at 24°. [g] Calc. on azlactone which reacted; 50% recovered unchanged. [h] Darkened somewhat on storage.

TABLE 2.

No.	Compound	Isomer *	Reduction	Cryst. from †	M. p.	$[\alpha]_D$	Yield (%)	Formula	Found (%) C	H	N	Cl	Required (%) C	H	N	Cl
1	IV; R = H	—	A	D [a]	171—172°	—	53	$C_{20}H_{22}O_2N_3Cl_2$	—	—	9·9	16·9	—	—	10·3	17·4
			B	D [b]	172—173 [c]	—	71	,,	59·0	6·0	10·3	16·9	58·8	5·6	10·3	17·4
2	IV; R = Et	—	B	E [a]	168—169 [d]	—	92	$C_{22}H_{27}O_2N_3Cl_2$	60·5	6·4	—	15·9	60·5	6·2	—	16·3
3	IV; R = *cyclo*hexyl	—	C	F [a]	181 [a]	—	—[f]	$C_{26}H_{33}O_2N_3Cl_2$	63·6	6·85	8·3	—	63·7	6·7	8·6	—
4	V; R = R′ = H	—	A	E [g]	212—213	—	65	$C_{23}H_{25}O_4N_3Cl_2$	56·7	5·3	8·6	—	56·65	5·4	9·0	—
			B	E [g]	211—213 [e]	—	84	,,	—	—	—	—	—	—	—	—
5	V; R = Me; R′ = H	DL	A	D [g]	212—213	—	55	$C_{33}H_{27}O_4N_3Cl_2$	57·0	5·55	8·7	14·6	57·5	5·6	8·75	14·8
			B	E [g]	215 [h]	—	76	,,	—	—	—	—	—	—	—	—
6	V; R = Me; R′ = H	L	A	G [a]	184—187	0° ± 1° [i]	31	,,	—	—	—	—	—	—	—	—
			B	E [a]	186—188 [e]	0 ± 1° [j]	57	,,	57·9	5·6	8·6	—	57·5	5·6	8·75	—
7	V; R = $Me_2CH{\cdot}CH_2$; R′ = Et	L	B	F [a]	149—150	0 ± 1° [k]	68	$C_{28}H_{27}O_4N_3Cl_2$	61·6	6·9	—	13·0	61·1	6·7	—	12·9
8	V; R = $PhCH_2$; R′ = Et	DL	A	E [a]	152—153	—	70	$C_{31}H_{25}O_4N_3Cl_2$	63·8	6·15	6·9	12·1	63·7	6·0	7·2	12·2

* The configuration given is that of the amino-acid attached to the N^{α}-benzoyl-*p*-di-(2-chloroethyl)amino-DL-phenylalanyl group. † All colourless or almost colourless.

A, Catalytic over Pt, Pd, and Ni. B, By Zn–acid. C, Catalytic over Raney Ni alone. D, Methanol. E, Aqueous methanol. F, Aqueous ethanol. G, Aqueous acetic acid. [a] Rods or needles. [b] Plates. [c] Unchanged on admixture with preceding compound. [d] Partial melting and resolidification, 152—156°. [e] Shrinkage and softening at 162°, then resolidification. [f] Not recorded. [g] Prisms. [h] Mixed m. p. with preceding compound, 212—213°. [i] *c* 1·5 in EtOH at 21°. [j] *c* 0·79 in EtOH at 22°. [k] *c* 1·31 in dioxan at 22°.

7·2; Cl, 18·3%). Moistening these with a little benzene caused the colour of the compound to revert to bright red. Both solid forms showed strong fluorescence under ultraviolet light.

2-Benzyl-4-[p-di-(2-chloroethyl)aminobenzylidene]thiazol-5-one (VI) (cf. Abraham *et al.*[7]).—Phenyl(thioacetyl)glycine [8] (2·09 g.), *p*-di-(2-chloroethyl)aminobenzaldehyde [3] (2·46 g., 1·0 mol.), and acetic anhydride (5 ml.) were shaken with gentle warming until dissolution was complete, then kept at 50—60° for 3 hr. After cooling, a solid was deposited; this was collected and washed with ethanol, then light petroleum. The orange rods (2·09 g., 50%), m. p. 153—155°, were recrystallised from benzene–ethanol, then Cellosolve, and yielded the *thiazolone* (1·6 g., 38%), m. p. 157—158° (Found: C, 60·2; H, 5·1; N, 6·5; S, 7·3; Cl, 16·8. $C_{21}H_{20}ON_2SCl_2$ requires C, 60·15; H, 4·8; N, 6·7; S, 7·6; Cl, 16·9%). The use of anhydrous sodium acetate and of a higher reaction temperature offered no advantage.

α-[p-*Di*-(2-*chloroethyl*)*aminobenzylidene*]*hippuramides* (II).—A concentrated aqueous solution of ammonia or of diethylamine (≮3 mol. equiv.) was added to an acetone solution containing the oxazolone (I; R = Ph) (0·5—1·0 g. per 10 ml.). The ammonia reaction was carried out at room temperature and was complete within 15 min. The ethylamine reaction mixture was heated under reflux for a few minutes. Reaction with *cyclo*hexylamine was carried out by heating under reflux a solution of the oxazolone (I; R = Ph) and base (3 mol. equiv.) in ethyl acetate for *ca.* 1 hr. The fading of the initial orange colour of the solution to lemon-yellow was a guide to the rate of reaction in all cases. The mixtures were evaporated to dryness under reduced pressure and the *amides* were crystallised from suitable solvents (Table 1).

α-[p-*Di*-(2-*chloroethyl*)*aminobenzylidene*]*hippuramido-acids and -amido-esters* (III; R′ = H *or* Et).—(a) *Reaction of oxazolone* (I; R = Ph) *with amino-acids.* The oxazolone was dissolved in boiling acetone (*ca.* 10 ml. per mmol. of oxazolone) and treated with a solution of the amino-acid (3 mol.) in N-sodium hydroxide (3 equiv.). The mixture was heated under reflux for 15 min., by which time the colour had usually faded to pale yellow. Most of the acetone was evaporated under reduced pressure, the residual aqueous solution diluted with a few ml. of water, and the product precipitated by addition of dilute hydrochloric acid to pH *ca.* 3. The products which could be purified by crystallisation are tabulated in Table 1.

(b) *Reaction of oxazolone* (I; R = Ph) *with amino-acid ethyl esters.* The oxazolone was refluxed for up to 1 hr. in ethyl acetate with the amino-ester (5 mol.; usually prepared from the ester hydrochloride by treatment with triethylamine in chloroform). The solution was evaporated, and the residue washed with dilute (*ca.* 0·1N-)hydrochloric acid to remove excess of amino-ester. Products obtained crystalline are given in Table 1.

α-[p-*Di*-(2-*chloroethyl*)*aminobenzyl*]-*hippuramides and -hippuramido-acids and -esters* (IV *and* V).—(a) *Catalytic reduction.* The unsaturated compound was shaken in methanol or methanol–ethyl acetate over Adams platinum oxide catalyst, Raney nickel, and 5% palladium–charcoal. The *cyclo*hexylamide (II; R = C_6H_{11}) was successfully reduced in the presence of Raney nickel alone. The results are set down in Table 2.

(b) *Chemical reduction.* The unsaturated compound (1 mmol.) was dissolved in glacial acetic acid (10 ml.), and concentrated hydrochloric acid (3 ml.) was added. Zinc dust (2 g.) was then added in two or three portions to the stirred and cooled solution. Stirring was continued for 10 min., though the colour of the solution generally disappeared within about 3 min. The mixture was filtered, the residual zinc washed with a little acetic acid, and the combined filtrate and washings were diluted with water to about 30 or 40 ml. The solution was brought to pH *ca.* 3 by the addition of N-sodium hydroxide, and the precipitated product was crystallised. The results are given in Table 2.

Hydrolysis of Reduced Peptides of L-*Alanine and of* L-*Leucine Ethyl Ester.*—(a) L-*Alanine derivative* (V; R = Me, R′ = H). The compound (101 mg.) was heated for 3 hr. under reflux in 6N-hydrochloric acid (2 ml.). Colourless needles, presumably benzoic acid, collected in the condenser. The solution was cooled and filtered from benzoic acid, and the filtrate and washings were made up to 2·1 ml. with 6N-acid. Mean α_D^{25} was $+0{\cdot}10° \pm 0{\cdot}03°$. Hence, for the alanine released (18·8 mg., assuming complete hydrolysis), $[\alpha]_D^{25} = +11° \pm 3°$ (*c* 0·935 in 6N-HCl). The L-alanine used had $[\alpha]_D^{25}$ $+11° \pm 1°$ (*c* 1·0 in 6N-HCl).[9]

(b) L-*Leucine derivative* (V; R = $Me_2CH{\cdot}CH_2$, R′ = Et). An experiment similar to the above in which the reflux time of the compound (50 mg.) in 6N-hydrochloric acid (1·5 ml.) was

[7] Abraham, Baker, Chain, and Robinson, "Chemistry of Penicillin," ed. Clarke, Princeton Univ. Press, 1949, p. 848.

[8] *Idem, op. cit.*, p. 778.

4 hr. gave a solution (final vol., 1·5 ml.) whose α_D^{25} was $+0·09° \pm 0·015°$. Hence, for the leucine released (11·9 mg., assuming complete hydrolysis), $[\alpha]_D^{25} = +11·5° \pm 2°$ (*c* 0·79 in 6N-HCl). The L-leucine used had $[\alpha]_D^{25} +16° \pm 2°$ (*c* 0·64 in 6N-HCl).[9]

We thank Professor A. Haddow for permission to use his biological results. This and related work has been supported by grants to this Institute from the British Empire Cancer Campaign, the Jane Coffin Childs Memorial Fund for Medical Research, the Anna Fuller Fund, and the National Cancer Institute of the National Institutes of Health, U.S. Public Health Service.

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FULHAM ROAD, S.W.3. [*Received, June 21st*, 1957.]

[9] Cf. Greenstein, Birnbaum, and Otey, *J. Biol. Chem.*, 1952, **204**, 207.

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918. *The Mechanism of Oxidation of α-Glycols by Periodic Acid. Part II.* Propane-1 : 2-, 2-Methylpropane-1 : 2-, Butane-2 : 3- and 2-Methylbutane-2 : 3-diol.*

By G. J. BUIST, C. A. BUNTON, and J. H. MILES.

The kinetics of oxidation of propane-1 : 2-, 2-methylpropan-1 : 2-, (−)- and *meso*-butane-2 : 3-, and 2-methylbutane-2 : 3-diol by periodic acid, in water at 0°, have been followed over a wide pH range. An intermediate is formed from periodic acid and the glycol, and decomposes to the products. For a given glycol the variations of the equilibrium constant, *K*, for the formation of the intermediate, and the rate constant, *k*, for its decomposition to products, can be observed and understood.

The general effect of methyl-substitution in the α-glycol is to increase the rate constant, *k*. The effect on the equilibrium constant, *K*, is two-fold: electron-release increases the equilibrium constant, but steric effects may decrease it. The latter depend on the stereochemistry of the glycol, *e.g.*, there is a steric repulsion between one of the methyl groups and an oxygen atom in the intermediate formed between *meso*-butane-2 : 3-diol and periodic acid, but not in that from the (−)-isomer.

IN Part I of this series * the oxidation of ethanediol by periodic acid was studied over a wide range of pH. We now describe an extension of this work to some methyl-substituted α-glycols. From the kinetic form for the oxidation of ethanediol (in large excess) Duke [1] showed that an intermediate was formed rapidly, and in high concentration, and that it slowly decomposed to the products, *viz.*:

$$\begin{matrix}CH_2{\cdot}OH\\ |\\ CH_2{\cdot}OH\end{matrix} + H_5IO_6 \overset{K}{\rightleftharpoons} \text{Intermediate} \overset{k\ (\text{Slow})}{\rightleftharpoons} 2CH_2O + HIO_3 + 2H_2O$$

This reaction sequence requires the kinetic law:

$$1/k' = 1/kK[G] + 1/k \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where k' is the first-order rate constant with respect to periodic acid, and [G] the glycol concentration. The oxidation of ethane- and other diols [2] was found to fit this kinetic form, and values of the constants *k* and *K* were determined. No effect of acidity on rate was considered, and for all the reactions in which the kinetic law (1) was obeyed it was assumed that the intermediate and the reactants were in equilibrium, *i.e.*, that the rates

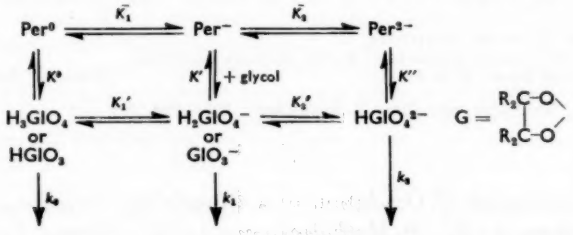
* Part I, *J.*, 1954, 1406.

[1] Duke, *J. Amer. Chem. Soc.*, 1947, **69**, 3054.
[2] Duke and Bulgrin, *ibid.*, 1954, **76**, 3803.

of formation of the intermediate, and of decomposition to the reactants, were much faster than the rate of decomposition to the products. For certain of the reactions studied this assumption is incorrect, as is shown in our subsequent papers.

Any interpretation of the kinetic data must take into account the equilibrium between the various species of periodic acid,[3] and between the various intermediates formed by co-ordination of a glycol molecule with periodic acid or its ions (Part I).

The equilibrium and rate constants can be related, as shown in the annexed scheme,



where Per^0, Per^-, and Per^{2-} represent the totality of the various periodate species, for the charges represented.

In Part I it was shown that to a good approximation k_0 and k_2 could be neglected, *i.e.*, only the singly negatively charged intermediate decomposes to products. With this simplification the rate constant, k, takes the forms:

$$pH > 5,\ k = k_1/(1 + K_2'f_{i^-}/a_{H^+}f_{i^{2-}}) \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

or

$$\log K_2' + pH + \log f_{i^-}/f_{i^{2-}} = \log(k_1/k - 1) \quad . \quad . \quad . \quad . \quad (2a)$$

$$pH < 5,\ 1/k = 1/k_1 + f_{i^-}a_{H^+}/K_1'k_1 \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where a_{H^+} is the hydrogen-ion activity determined with a glass electrode, and f_{i^z} are the activity coefficients of the z-charged ions. The assumptions involved in the deduction of these equations are discussed in Part I.

The equilibrium and apparent dissociation constants can be similarly related; *e.g.*, for solutions of pH <5:

$$K = \frac{\bar{K}_1(K' - K)}{f^-a_{H^+}} + \frac{K'\bar{K}_1}{K_1'} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

These relations were deduced from observations on the oxidation of ethanediol (Part I). They apply equally to the oxidations of propane-1 : 2-, 2-methylpropane-1 : 2-, and *meso*-butane-2 : 3-diol over the whole pH range, and to the oxidations of (−)-butane-2 : 3- and 2-methylbutane-2 : 3-diol over certain pH ranges,[4] and in this paper we restrict our attention to systems in which intermediate and reactants come into equilibrium. These relations do not apply to the oxidation of pinacol; this will be the subject of a later communication.

As an example of the results we show a plot of eqn. (2*a*) (Fig. 1). The slope should be, and is, independent of glycol structure, and close to unity. Values of the equilibrium constants are given in Table 1, and those of the rate constants for the breakdown of the single negatively charged intermediates in Table 2.

There are certain omissions from Table 1. These, which apply to the oxidations of (−)-butane-2 : 3- and 2-methylbutane-2 : 3-diol at pH 4—5, arise because the underlying assumption of equation 1, that both the conversion of the reactants into the intermediate and its breakdown to regenerate the reactants are much faster than decomposition to the products, is not always correct. If the reactants and intermediate are not in equilibrium the numerical values of K and k [equation (1)] may be incorrect. There are several methods

[3] Crouthamel *et al.*, *J. Amer. Chem. Soc.*, 1949, **71**, 3031; 1951, **73**, 82.
[4] Buist, Bunton, and Shiner, *Research*, 1953, **6**, 45.

by which this equilibrium requirement can be tested. It may be possible to verify by physical measurements, *e.g.*, electrochemical (Part I) or spectrophotometric (subsequent paper), that the formation of the intermediate is an equilibrium reaction. Further evidence can sometimes be obtained by a careful study of the kinetic form. In the oxidations of (−)-butane-2 : 3- and 2-methylbutane-2 : 3-diol at pH 4—5 an induction period can be observed: this corresponds to a slow build up of the intermediate. Here

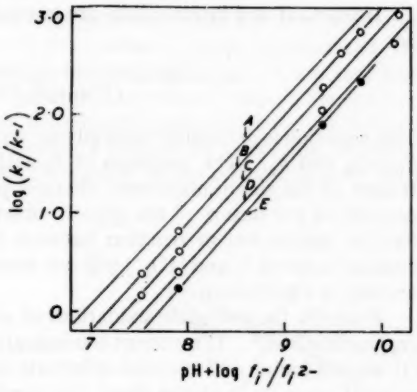


FIG. 1. *Relation between rate constant and* pH. *Diols*: *A*, *ethane-*; *B*, *propane-*1 : 2- *and* meso-*butane-*2 : 3-; *C*, (−)-*butane-*2 : 3-; *D*, 2-*methylpropane-*1 : 2-; *E*, 2-*methylbutane-*2 : 3-.

also equation (1) is not obeyed, *i.e.*, a plot of $1/k'$ against $1/[G]$ may not give a straight line. There are, however, cases where equilibrium is not maintained, but the above discrepancies are not observed.

TABLE 1. *Equilibrium and dissociation constants* (*mole*$^{-1}$ *l.*) *of the intermediates.*

Diol	K^0	K'	K''	$10^2K_1'$	$10^7K_2'$
Ethane- [a]	10	189	1800	17·4	1·1
Propane-1 : 2-	39	500	2800	5·0	0·65
meso-Butane-2 : 3-	19 [b]	68 [b]	373	2·6	0·50
(−)-Butane-2 : 3-	270	—	8000	3·4	0·42
2-Methylpropane-1 : 2-	16	101	360	2·6	0·28
2-Methylbutane-2 : 3-	60	—	940	1·4	0·19

[a] Part I. [b] It is difficult to verify the equilibrium conditions here. The first and second dissociation constants of periodic acid are: by direct measurement, $3·6 \times 10^{-3}$ and $1·2 \times 10^{-8}$ respectively, and by analysis of the kinetic data, $4·0 \times 10^{-3}$ and $1·2 \times 10^{-8}$.

TABLE 2. *Rate constants for decomposition of single negatively charged intermediate.*

Diol	Ethane- [a]	Propane-1 : 2-	*meso*-Butane-2 : 3-	(−)-Butane-2 : 3-	2-Methylpropane-1 : 2-	2-Methylbutane-2 : 3-
10^4k_1 (sec.$^{-1}$) ...	45·7	120	182	302	607	244

[a] Part I.

A more sensitive test comes from rate studies in which the concentrations of reactants are sufficiently low for the concentration of the intermediate to become negligible in comparison with them. On these conditions the stationary-state approximation can be used and then for the reaction:

$$\text{Glycol} + \text{Periodate} \underset{k_b}{\overset{k_f}{\rightleftharpoons}} \text{Intermediate} \xrightarrow{k} \text{Products}$$

we can write:

$$v = k_s[G][Per] = kk_f[G][Per]/(k_b + k) \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

i.e.,

$$k_s = k_f/(1 + k_b/k) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5a)$$

where k_s is the limiting second-order rate constant, and k_f and k_b are second- and first-order rate constants for the forward and back reactions involved in formation of the intermediate. For equilibrium $k_b/k \gg 1$, and $K = k_f/k_b$, and so $k_s = kK$; *i.e.*, the reciprocal of k_s should equal the slope of the line obtained by plotting $1/k'$ against $1/[G]$ [equation (1)].[2] If equilibrium conditions are not maintained, *i.e.*, if k_b/k is not much greater than 1, then $1/k_s$ will be greater than the slope of the " reciprocal plot " (eqn. 1). The conditions in which this test can be applied are discussed in a subsequent paper.

If reactant and intermediate are in equilibrium, the limiting second-order rate constant is:

$$k_s = kK = \frac{k_1K'}{(f^-a_{H^+}/K_1) + 1 + (f^-K_2/f^{2-}a_{H^+})} \propto \frac{[Per^-]}{[Per]} \quad . \quad . \quad . \quad (6)$$

This equation is derived by multiplying equations (7) and (9) of Part I, and assuming that $k_1 \gg k_0$ and k_2. The variation of k_s with pH will therefore follow the relative concentration of the singly negatively charged periodate ions, and hence of IO_4^-, and be independent of the nature of the glycol; observation of this correlation can give no evidence for the mechanism of reaction between the glycol and periodic acid (cf. ref. 5). This relation between k_s and $[IO_4^-]$ will not necessarily be true if the reactants and intermediate are not in equilibrium.

Recently the periodate oxidations of several α-glycols have been followed by a polarographic method.[6] The reagent concentrations were so low that the kinetic form of equation (1) was not found, and a second-order rate law applied [equation (5*a*)]. Such an observation of itself gives no evidence about the mechanism of oxidation.

Summary of Kinetic Data.—It was arbitrarily assumed that the equilibrium conditions were satisfied when $k_b/k > 10$. This was so for the oxidations of propane-1 : 2-, 2-methylpropane-1 : 2-, and *meso*-butane-2 : 3-diol at all acidities examined (and for ethanediol; Part I). Equilibrium conditions were not satisfied for the oxidation of (−)-butane-2 : 3- and 2-methylbutane-2 : 3-diol in the region pH 4—5. Deviation from equilibrium is particularly marked for the latter compound. The equilibrium and rate constants of Tables 1 and 2 were calculated by the methods outlined in Part I. These constants, unlike those derived from equation (1), are independent of pH.

Discussion of Variations of Equilibrium and Rate Constants.—Dissociation constants of the intermediates. With increasing methyl-substitution K_1' and K_2' (the apparent first and second dissociation constants of the intermediate) decrease regularly. This could be due to inductive electron-release by the methyl groups. The effect of two methyl groups on the same carbon atom is greater than that of two methyl groups on different carbon atoms. As would be expected, the intermediates are stronger acids than periodic acid itself, the acid strength decreasing with increase in the number of methyl groups.

Equilibrium constants for formation of the intermediate. It is not easy to relate structural changes with K^0 and K' (the constants relating the reactants and the neutral and singly negatively charged intermediates respectively), because these two intermediates may exist in hydrated or dehydrated forms (Part I), as may periodic acid itself.[3] This difficulty does not arise if we restrict our attention to the doubly negatively charged intermediate, because this must exist in the hydrated form (this is probably, but not certainly also true of the neutral intermediate).

The equilibrium constants follow the sequence: ethane- < propane-1 : 2- < (−)-butane-2 : 3- > *meso*-butane-2 : 3- ≈ 2-methylpropane-1 : 2- < 2-methylbutane-2 : 3-diol. This requires the effect of methyl-substitution to be, at least, two-fold. We suggest that inductive electron-release by the methyl groups increases the stability of the intermediate (relatively to that of the reactants) by increasing the electron-availability at the oxygen bonds. There is also an obvious steric effect: this can be seen by comparing the

[5] Taylor, *J. Amer. Chem. Soc.*, 1953, **75**, 3912.
[6] Zuman, Sicher, Kmpicka, and Svoboda, *Nature*, 1956, **178**, 1407.

values for 2-methylpropane-1 : 2- and butane-2 : 3-diol. Inspection of molecular models shows that there may be steric pressure between the methyl groups and one or more of the oxygen atoms in the intermediate. Molecular models of the hypothetical cyclic intermediate were constructed, using the dimensions of the Stuart models for carbon, oxygen, and hydrogen and the dimensions of ammonium trihydrogen paraperiodate, $(NH_4)_2H_3IO_6$, as determined by *X*-ray crystallography.[7] In this compound iodine is octahedral with iodine–oxygen distances of 1·93 Å.

It is improbable, from consideration of molecular geometry, that the five-membered ring of the presumed intermediate is planar. If the carbon–carbon distance and the carbon bond angles are assumed to be unchanged in the intermediate, such a planar ring would require the oxygen–oxygen distance to be smaller, and the oxygen–iodine–oxygen bond angle to be greater than in ammonium trihydrogen paraperiodate. It seemed probable therefore that the strain of such a ring would be reduced by puckering, as shown in Fig. 2, where the plane through the iodine and the carbon atoms of the ring is at right

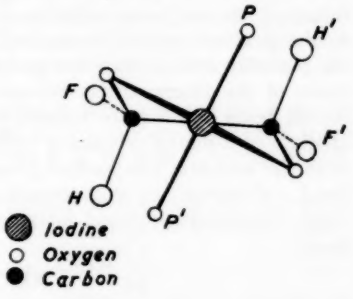


FIG. 2. *Model of the intermediate complex (two oxygen atoms omitted).*

angles to the plane of the paper, the two carbon atoms are in the plane of the paper, and the iodine atom and the " glycol " oxygen atoms are above it. Two of the oxygen atoms attached to the octahedral iodine atom are omitted (for clarity); they lie towards the observer, in positions equivalent to *P* and *P'*. Methyl groups may occupy any of the four positions, *F* and *F'*, and *H* and *H'*. Examination of molecular models shows that the two equivalent positions *F* and *F'* (free positions) are not near to any of the oxygen atoms, but that there is some compression between the oxygen atoms and methyl groups in the equivalent positions, *H* and *H'* (hindered positions). If we consider methyl-substitution in the intermediate formed between ethanediol and periodic acid, we find that for both propane-1 : 2-, and (—)-butane-2 : 3-diol the methyl groups may be in free positions, *F* and *F'*. But 2-methylpropane-1 : 2-, *meso*-butane-2 : 3-, and 2-methylbutane-2 : 3-diol must have one methyl group in a hindered position, *H* or *H'*, with consequent compression, and a lowering of the equilibrium constant. Pinacol must have two methyl groups in hindered positions, and the equilibrium constants for formation of its intermediates would therefore be low.

Structures other than this cyclic form have been proposed for the intermediates between glycols and glycol-splitting reagents (see, for example, Criegee *et al.*[8]). In most of these only one of the hydroxyl-oxygen atoms is bonded directly to the iodine atom, the other being bonded through a hydrogen atom, to an oxygen atom of the oxidising agent or to some other entity. Such structures may well exist, particularly with reagents such as lead tetra-acetate which are used in non-aqueous solutions and are less specific in their reactivity than is periodic acid. However the five-membered cyclic intermediate seems to us to be the only formulation which will explain the effects of changes in the

[7] Helmholtz, *J. Amer. Chem. Soc.*, 1937, **59**, 2036.
[8] Criegee, Höger, Huber, Kruck, Marktscheffel, and Schellenberger, *Annalen*, 1956, **599**, 81.

glycol structure on the formation and breakdown of the intermediate, and the fact that only the singly negatively charged intermediate decomposes to the products.

We can therefore analyse the experimental sequence for the equilibrium constant, K'', in terms of the two sequences. (*a*) Increasing polar effect, no hindered methyl groups: ethane- < propane-1 : 2- < (−)-butane-2 : 3-diol. (*b*) Increasing steric compressions: (−)-butane-2 : 3- > *meso*-butane-2 : 3- ≃ 2-methylpropane-1 : 2-diol. 2-Methylbutane-2 : 3-diol, with three methyl groups, one in a hindered position, shows these opposing steric and polar effects. Comparison between K'' for *meso*- and (−)-butane-2 : 3-diol (Table 1) shows that a hindered methyl group in the intermediate reduces the equilibrium constant *ca.* 20-fold. Thus the expected value of K'' for pinacol would be much less than that of 2-methylbutane-2 : 3-diol, particularly because steric effects are intensified with increased overcrowding. It seems unlikely that this equilibrium constant can be determined experimentally for pinacol (cf. ref. 2).

Rate constant for decomposition of the intermediate to the products. The values of k_1 (Table 2) increase with increasing methyl-substitution in the glycol (except for *meso*-butane-2 : 3- and 2-methylbutane-2 : 3-diol). The rate of breakdown of the intermediate to the products should be assisted by hyperconjugation between the methyl groups and the partially formed carbonyl groups. This does not explain the different rates of breakdown of the intermediates formed from the three butanediols. If one carbon–oxygen double bond began to be formed before the other the faster decomposition of the intermediate of 2-methylpropane-2 : 3-diol than of the butane-2 : 3-diols would be explained, as in the first case two methyl groups would be hyperconjugated with the forming double bond. However, all such considerations are complicated by the possibility that the singly negatively charged intermediate may exist in hydrated (*a*) and dehydrated (*b*) forms:

It has been suggested that only the dehydrated form (*b*) decomposes to the products (Part I). If this is so, the rate of decomposition will depend on the relative amounts of these two forms, and this in turn, to an extent at present unknown, on the groups present.

The results described here are in complete agreement with the demonstration that only the singly negatively charged intermediate decomposes to the reaction products (Part I). On this hypothesis it is possible to calculate the equilibrium constants for formation of the intermediate, its acid dissociation constants, and its rate constant for decomposition, provided it is known, from experiment, that in any given reaction the reactant and intermediate are in equilibrium. Examples of the kinetic form of oxidations in which this equilibrium condition does not hold will be given in a subsequent paper.

Experimental

Materials.—Propane-1 : 2- and (−)-butane-2 : 3-diol were purified by vacuum-distillation of commercial samples. Propane-1 : 2-diol had n_D^{25} 1·4315; (−)-butane-2 : 3-diol had m. p. 19°, n_D^{24} 1·4310, 1·4312, $[\alpha]_D^{20}$ −12·84°, −12·68°.

meso-Butane-2 : 3-diol was isolated from a commercial sample of butane-2 : 3-diol by fractionation under reduced pressure and recrystallisation of the hydrate; after dehydration it had m. p. 33·6—34·4°, n_D^{25} 1·4371 (supercooled), and no optical activity.

2-Methylpropane-1 : 2- and 2-methylbutane-2 : 3-diol were prepared by the osmium tetroxide-catalysed oxidation of the corresponding olefin with *tert.*-butyl hydroperoxide.[9] 2-Methylpropane-1 : 2-diol had b. p. 84—85°/14 mm., n_D^{25} 1·4330. 2-Methylbutane-2 : 3-diol hydrate had m. p. 22·0—22·7° (unchanged by further recrystallisation). Dehydration gave the glycol with b. p. 84—85°/19 mm., n_D^{25} 1·4363. A sample of this glycol obtained in poor yield by oxidation of trimethylethylene with peracetic acid had physical properties identical with those given above, and was oxidised at the same rate as the other sample.

[9] Milas and Sussman, *J. Amer. Chem. Soc.*, 1936, **58**, 1302.

The periodate and buffer solutions were prepared and used as described in Part I. Here, and subsequently, the concentration of glycol is that at half reaction, except for runs in which reactant concentrations are similar.

Rate Measurements.—Most reactions were followed by the general methods described in Part I. However, some oxidations were too fast for conventional sampling methods to be used. An automatic pipette, based on the well-known " self-filling " pipette, was therefore made. It was kept at a constant temperature by circulating ice-water through its jacket. It could be filled, and its contents expelled, by compressed air, and could deliver up to 11 samples per min. Faster runs with pH < 4 were quenched in alkali to stop the reaction rapidly, the pH was then adjusted to 8, with saturated aqueous sodium hydrogen carbonate, for analysis of periodate. In one case, that of (−)-butane-2 : 3-diol at pH 5, it was necessary to use a spectrophotometric method for following the first part of the run.

First-order rate constants were calculated graphically, from the usual integrated form. Second-order rate constants were calculated graphically from the equation $k_2t(b - a) = 2{\cdot}3 \log\{a(b - x)/b(a - x)\}$, where a and b are the initial concentrations of the reactants, and x is the extent of reaction, in the same units. When a and b were of similar magnitude the second-order rate equation was used in its expanded approximate form. In one case [oxidation of (−)-butane 2 : 3-diol], the limiting second-order rate constant, k_s, could not be obtained with reactant concentrations sufficiently high for determination by titration; the concentration of periodate was therefore obtained spectrophotometrically.[3] All first-order rate constants are in sec.$^{-1}$, and all second-order are in sec.$^{-1}$ mole^{-1} l.

Summary of Kinetic Results.—No departure from equilibrium behaviour was found for the oxidations of propane-1 : 2-, 2-methylpropane-1 : 2-, and *meso*-butane-2 : 3-diol, but there were marked deviations from equilibrium in the region pH 4—5 for both (−)-butane-2 : 3- and 2-methylbutane-2 : 3-diol.

In general the value of the limiting second-order rate constant, k_s (equation 5*a*), was determined at pH 1 and *ca.* 5. This was done by progressively decreasing the reactant concentrations until a constant value of the second-order rate constant was reached. Observation of a straight line for a plot of log $(b - x)/(a - x)$ against time is not a sensitive test for a second-order kinetic form (cf. ref. 2): it is in general impossible to determine kinetic order from the results of a single run.

Propane-1 : 2-diol. The evidence for equilibrium is: At pH 1·0, the limiting second-order rate constant $k_s = 0{\cdot}214$ (for 10^4[G] = 3·70M and 10^4[Per] = 5·99M, the value kK calculated from equation 1 = 0·234). At pH 5·4, 8·8, and 9·12 spectrophotometric measurements show that k_f and $k_b \gg k$.

pH	0·99	1·37	1·76	1·94	4·48	5·58	7·20	7·53	9·19	9·41
I *	0·130	0·054	0·148	0·01	0·021	0·055	0·087	0·129	0·130	0·102
10^4k	43·7	72·5	102	102	120	112	35·7	16·1	0·282	0·170
K	56	59	109	110	500	490	850	—	—	—

* Ionic strength in mole l.$^{-1}$.

2-Methylpropane-1 : 2-diol. The evidence for equilibrium is: pH 1·0, $k_s = 0{\cdot}280$ (the value of kK calculated from equation 1 is 0·302). At higher pH values spectrophotometric measurements show that k_f and $k_b \gg k$.

pH	0·99	1·37	5·44	7·53	9·04	9·78
I	0·130	0·054	0·104	0·129	0·100	0·100
10^4k	149	270	596	177	5·54	1·12
K	20·7	20·4	103	232	350	360

meso-*Butane-2 : 3-diol.* The evidence for equilibrium is: pH 1·4, $k_s = 0{\cdot}80$ sec.$^{-1}$ mole^{-1} l. (from equation 1, $kK = 0{\cdot}82$). At pH 4·48, $k_s = 1{\cdot}23$ and $kK = 1{\cdot}25$ (this is not a sensitive test because K is low). At pH 7·13, $k_s = 0{\cdot}943$, and $kK = 0{\cdot}833$.

pH	0·99	4·48	7·13	9·17
I	0·130	0·021	0·123	0·100
10^4k	44·0	182	70·9	0·568
K	18·6	68·2	118	373

XUM

(−)-*Butane* 2 : 3-*diol*. At pH 1·0, $k_a = 3{\cdot}2$ and $kK = 3{\cdot}2$. At pH > 9 spectrophotometric measurements (following paper) show that k_f and $k_b \gg k$, *i.e.*, at both high and low pH reactants and intermediate are in equilibrium. This is not so for reaction at pH 5·44. Here the initial part of the reaction was followed spectrophotometrically (Fig. 3). There is a slow build up of the intermediate, and k_b does not greatly exceed k. The value of $k_a = 26$, but the slope of the " reciprocal " plot (equation 1) = 5·9, *i.e.*, reactants and intermediate are not in

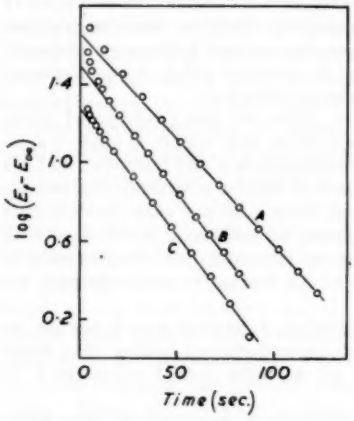


FIG. 3. *Oxidation of* (−)-*butane*-2 : 3-*diol at* pH 5·4.

A, [G] = 3 × 10⁻³M. *B*, [G] = 10⁻³M. *C*, [G] = 3 × 10⁻³M.

equilibrium. The initial reactant concentrations of *ca.* 10^{-5}M were too low for chemical methods of analysis, and therefore spectrophotometric methods were used.

pH	0·99	1·37	5·44	7·20	7·53	9·04	9·79
I	0·130	0·054	0·104	0·087	0·129	0·100	0·121
10^4k	94	151	300	126	61·5	1·58	0·282
K	370	320	*	*	—	*ca.* 10^5	*ca.* 8 × 10^4

* The " apparent " value of *K*, from the slope of the " reciprocal " plot (equation 1), is *ca.* 2000.

2-*Methylbutane*-2 : 3-*diol*. The kinetic form of the oxidation was not determined in detail over the whole pH range. At pH 1·0, $k_a = 0{\cdot}245$ and $kK = 0{\cdot}247$. At pH > 9, spectrophotometric measurements (following paper) showed that the reactants and intermediate are in equilibrium. Therefore equilibrium conditions are satisfied, at high and low values of pH. The results at pH 4·5 provided an excellent example of a periodic acid oxidation in which the reactants and intermediate are not in equilibrium. The breakdown of the intermediate to the products is in fact *ca.* 3 times as fast as to the reactants; this kinetic form will be discussed in detail in a subsequent paper.

pH	0·99	1·37	4·48	7·53	9·04	9·41
I	0·130	0·054	0·021	0·129	0·100	0·102
10^4k	38·9	64·8	244	91·2	3·04	*ca.* 1
K	67	78	(250 *)	(400 *)	940	—

* These are " apparent " values from the slope of the " reciprocal " plot.

The authors are indebted to Professors E. D. Hughes, F.R.S., and C. K. Ingold, F.R.S., and Dr. V. J. Shiner for their interest in this work. They thank the University of London for a studentship (G. J. B.) and the Department of Scientific and Industrial Research for a maintenance allowance (J. H. M.).

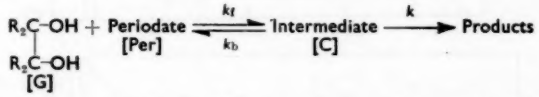
WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES, UNIVERSITY COLLEGE, GOWER ST., LONDON, W.C.1. [*Received, May 6th*, 1957.]

919. *The Mechanism of Oxidation of α-Glycols by Periodic Acid. Part III.*[1] *Spectroscopic Evidence for the Formation of an Intermediate.*

By G. J. Buist, C. A. Bunton, and J. H. Miles.

The reversible formation of an intermediate between periodic acid and and α-glycol is, for most glycols, faster than the irreversible decomposition of this intermediate to the products. For suitable systems this formation can be followed spectrophotometrically. For a series of open-chain α-glycols in the pH range 8·5—11·5 the relative rates of formation are: ethane- > propane-1 : 2- > 2-methylpropane-1 : 2- ≈ *meso*-butane-2 : 3- > (−)-butane-2 : 3- > 2-methylbutane-2 : 3-diol.

From a study of the kinetic form of the oxidation of some open-chain α-glycols it is possible to calculate both the equilibrium constant, K, for the formation of a cyclic intermediate and the first-order rate constant, k, for its breakdown to products.[1,2a,b] This evidence can give no information on the mechanism by which the intermediate is formed from, and breaks down to, the glycol and periodic acid, because this simple kinetic treatment can be applied only if the intermediate is in equilibrium with the reactants. *I.e.*, for the sequence:



the rate of decomposition to products, k[C], must be much less than k_f[Per][G] and k_b[C], and then $k_f/k_b = K$ (Part II). These conditions are not always fulfilled, and it is then sometimes possible to obtain values for k_f and k_b from the overall chemical kinetics. (This special case is discussed for the oxidation of 2-methylbutane-2 : 3-diol at pH 4—5, in the succeeding paper.)

It was noticed that the pH change on mixing of periodic acid and an α-glycol was faster than the oxidation, but was not instantaneous.[2b] This suggests that the formation of the intermediate is not instantaneous. It therefore seemed possible to follow this rapid formation of an intermediate by physical methods.

Addition of ethanediol to a periodate solution in the pH range 9—11, at 0°, gave a change in optical density, slow enough to be followed but much faster than the overall reaction. It was assumed that this initial change was due to the formation of the intermediate.

For a reaction with the glycol in excess the first-order rate constant for the interconversion of periodate into intermediate is:

$$k' = k_f[G] + k_b$$

Kinetic runs on the formation of the intermediate were carried out with several glycols, at various pH values, examples being shown in Fig. 1. The plots of the logarithms of $(E_\infty - E_t)$ *versus* time t (where E_t and E_∞ are the optical densities at times t and infinity) are straight lines. The slope of these straight lines give the values of k', and these when plotted against the glycol concentration give a straight line (Fig. 2). From such results we calculate values of k_f and k_b. It is necessary to show that these values have the significance which we attach to them. The intermediate and reactants are in equilibrium in all the conditions and with all the compounds studied by this spectrophotometric method. Therefore the ratio k_f/k_b, determined spectrophotometrically, should equal the equilibrium constant, K, determined by chemical kinetics (Part II). The agreement (Table 1) is reasonably good, within the rather large uncertainties of the observations.

[1] Part II, preceding paper.

[2] (*a*) Duke *et al.*, *J. Amer. Chem. Soc.*, 1947, **69**, 3054; 1956, **76**, 3803; (*b*) Buist, Bunton, and Shiner, *Research*, 1953, **6**, 45; Buist and Bunton, *J.*, 1954, 1406.

TABLE 1. *Comparison between k_f/k_b and the chemically determined equilibrium constant.*

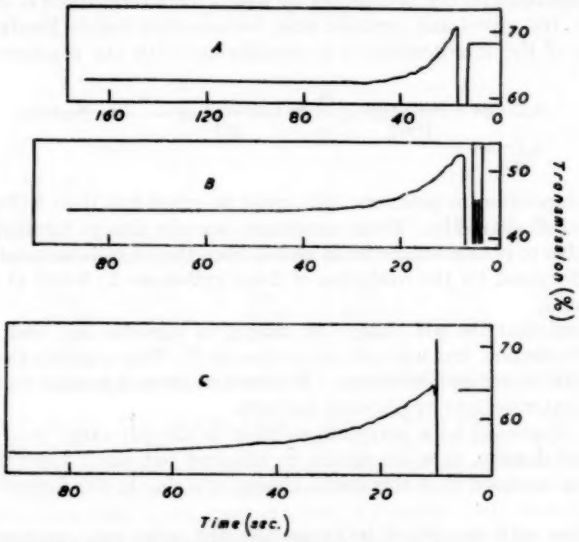
Diol	pH	k_f (sec.$^{-1}$ mole^{-1} l.)	$10^3 k_b$ (sec.$^{-1}$)	k_f/k_b (mole^{-1} l.)	K * (mole^{-1} l.)
Ethane-1 : 2-	10·6	14·7	930	1580	1800
2-Methylpropane-1 : 2-	10·6	1·82	700	260	360
meso-Butane-2 : 3-	9·25	28·9	91·2	317	373
2-Methylbutane-2 : 3-	0·95	5·33	89·0	60	67

The spectrophotometrically determined values of k_b differ slightly from the calculated values given in Table 2.

* Part II.

The intercepts of plots such as that shown in Fig. 2 give the values of k_b; it is not easy to determine these accurately, partly because an extrapolation to zero glycol concentration is required, but also because in many cases $k_f[G] \gg k_b$, and so the intercepts are near the origin. The slopes of the lines can be determined much more accurately, and it

FIG. 1. *Spectrophotometric traces showing formation of the intermediate.*



A, *Propane*-1 : 2-*diol*, pH 9·12, [G] = 1·01 × 10^{-3}M.
B, 2-*Methylpropane*-1 : 2-*diol*, pH 10·62, [G] = 5·11 × 10^{-3}M.
C, *Ethane*-1 : 2-*diol*, pH 10·62, [G] = 3·72 × 10^{-3}M.

is therefore convenient, in most cases, to determine k_b indirectly from the known values of k_f and K'', where K'' is the equilibrium constant for formation of the doubly negatively charged intermediate from the doubly negatively charged periodate and the glycol. This is the appropriate equilibrium constant for the region pH > 9·0 where these doubly negatively charged species predominate (Parts I and II). The calculation does of course require that the reactants and intermediate be in equilibrium (Part II).

There are considerable limitations to the spectrophotometric method for obtaining the rates of formation of the intermediate. First, at many pH values the formation of the intermediate is too fast for the recording equipment of the spectrophotometer. Secondly, if the rate of decomposition of the intermediate to the products is comparable with its rate of formation, a steady infinity value will not be reached. Under these conditions k_f and k_b cannot be calculated without knowledge of the extinction coefficients of all the chemical species involved, and it was not possible to determine these. Thirdly, at certain

pH values and wavelengths, the extinction coefficients of the intermediate and periodate are such that the change in optical density on mixing the reagents is too small for useful measurement.

However, within these experimental limitations the method gives positive information on the formation of an intermediate, and shows the effects of pH and structural changes on the rates of formation of the intermediates, mostly in the pH range 9—11.

Increasing methyl-substitution decreases the rates of formation of the intermediate (Fig. 3 and Table 2). This effect is probably steric, because the inductive effect of the methyl groups should increase the electron-density on the oxygen atoms of the glycol, and hence their ability to attack the iodine atom. Tracer evidence on the periodate oxidation of pinacol shows that the oxygen atoms of the product come from the pinacol itself.[2b]

FIG. 2. *Relation of spectrophotometric rate constants to glycol concentration.*

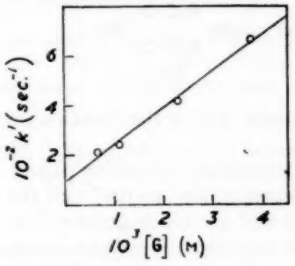
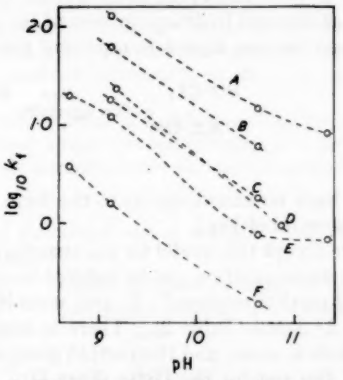


FIG. 3. *Rates of formation of intermediates.*



A, Ethane-1 : 2-*diol*; *B, propane*-1 : 2-*diol*; *C, 2-methylpropane*-1 : 2-*diol*; *D,* meso- *and E* (−)-*butane*-2 : 3-*diol*; *F, 2-methylbutane*-2 : 3-*diol.*

If, as seems probable, this is so for other glycols, the formation of the cyclic intermediate will be akin to esterification, in which the hydroxyl-oxygen atom will attack the iodine atom.

The rates of formation of the intermediates from *meso*- and (−)-butane-2 : 3-diol are very similar (Fig. 3 and Table 2), although the equilibrium constants for the formation of these intermediates are very different, that for the *meso*-isomer being the lower (Part II). This difference in stability is presumably due to the steric hindrance in the fully formed

TABLE 2. *Spectrophotometrically determined values of k_f, and calculated values of k_b (λ = ca. 2220 Å).*

Diol	Ethane			Propane-1 : 2-		2-Methylpropane-1 : 2-	
pH	9·1	10·6	11·3	9·1	10·6	9·1	10·6
k_f (sec.$^{-1}$ mole^{-1} l.)	130	14·7	8·4	62	6·2	18·1	1·82
$10^4 k_b$ (sec.$^{-1}$)	720	82	46	220	22	510	51
K''	1800			2800		360	

Diol	(−)-Butane-2 : 3-				*meso*-Butane-2 : 3-		2-Methylbutane-2 : 3-				
pH	8·7	9·1	10·6	11·3	9·25	10·9	0·11	0·95	8·7	9·1	10·6
k_f (sec.$^{-1}$ mole^{-1} l.)	20·5	12·0	0·78	0·69	28·9	0·91	4·8	5·3	3·8	1·6	0·15
$10^4 k_b$ (sec.$^{-1}$)	39	15	1·0	0·9	78	2·4			40	17	1·6
K''	8000				373				940		

TABLE 3. *Sequences of values of k_b and K'' with methyl-substitution.*

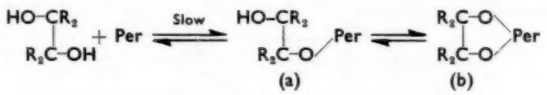
Substitution with no hindering methyl groups:

Inc. K'', dec. k_b: ethane- < propane-1 : 2- < (−)-butane-2 : 3-diol

Effect of hindering methyl groups:

Dec. K'', inc. k_b: (−)-butane-2 : 3- > *meso*-butane-2 : 3- > 2-methylpropane-1 : 2-diol

cyclic intermediate, but as there is no kinetic steric effect on the formation of the intermediate we must assume that the slow step of this formation is the attack of the first oxygen atom of the glycol on the iodine atom of the periodate. In partial confirmation of this, examination of molecular models suggests that there will be no difference between the steric effects of the methyl groups, for the two isomers, on this attack of the first oxygen atom. We therefore assume that in the formation of the cyclic intermediate the slow step is the formation of a monochelated intermediate (a), and that this ring closes rapidly to form the cyclic intermediate (b). It is probable that the dipoles between the carbon atoms and hydroxyl groups of the glycol will keep these groups in the *anti*-configuration, and we may therefore represent the formation of the cyclic intermediate as:



(As we have no knowledge as to the form of the periodic acid in this reaction we represent it by the symbol Per.)

If we accept this model for the structure of the intermediate (preceding paper), it follows that its decomposition can be subject to steric acceleration, and we find that the values of k_b for 2-methylpropane-1 : 2- and *meso*-butane-2 : 3-diol are much greater than for (−)-butane-2 : 3-diol (Table 2). There is steric pressure between the oxygen atoms attached to the iodine atom, and the methyl groups, in these cyclic intermediates of the two former glycols, but not for the latter (Part II). In confirmation of this, the sequence of values of k_b, for the various glycols, is similar to that of K'', the equilibrium constant relating the concentrations of the doubly negatively charged periodate ions, and the doubly negatively charged intermediate. It can be seen that this reaction sequence will give a very low concentration of the monochelated intermediate (a). This agrees with the observation that intermediates between periodic acid and monohydric alcohols have never been detected.[3]

In the pH range 8·5—11 an increase of pH decreases the rate of formation of the cyclic intermediate. This variation of k_f (and of k_b) with pH is almost independent of the glycol (Fig. 3). The values for the rates of formation of the cyclic intermediate of 2-methylbutane-2:3-diol have been estimated spectrophotometrically in solutions of pH < 1 and > 8·5, and by chemical methods at pH 4·48, where $k_f = 1{\cdot}9$ (sec.$^{-1}$ mole^{-1} l.) (succeeding paper). There must therefore be a rate maximum in the range of pH 4·5—8·5, and possibly in the range of pH 1—4·5. Such maxima are observed in the oxidation of pinacol,[3] and this makes it reasonable to accept the view that the rate of oxidation of pinacol is the rate of formation of an intermediate which rapidly breaks down to the products.

EXPERIMENTAL

A Cary recording spectrophotometer was used in all the experiments. Three different types of cell were used. One was of brass with windows of fused silica, and an evacuated jacket; it had an inner jacket which could be filled with crushed ice.[5] This construction had

[3] Crouthamel *et al.*, *J. Amer. Chem. Soc.*, 1949, **71**, 3031; 1951, **73**, 82.
[4] Price *et al.*, *ibid.*, 1938, **60**, 2726; 1942, **64**, 552, unpublished results, Buist and Miles.
[5] Passerini and Ross, *J. Sci. Instr.*, 1953, **30**, 274.

the grave disadvantage that the reaction mixture was in contact with brass, the usable pH range being thereby restricted. Therefore an all-quartz, vacuum-jacketed cell was obtained; in this design misting of the windows was avoided by a vacuum-jacket, and water at 0° was circulated in an inner jacket enclosing the cell. This cell was intended for general use at temperatures down to that of liquid air, but it succumbed to thermal strain at this temperature. A simpler version of this cell was therefore constructed with an outer brass water-jacket surrounding a fused-silica Cary cell; misting of the windows was avoided by an outer air space through which dry air was passed. The apparatus was lagged with asbestos. Temperature control was in the range 0—0·5°. The least reliable results are those with compounds whose equilibrium constant is low (because here the change in optical density is least) or in which the rate of formation of the intermediate is low.

The procedure for following the reaction was to fill the cell with a solution (10 c.c.) of periodate in the appropriate phosphate buffer at 0°. A small volume (0·02—0·20 c.c.) of a concentrated aqueous solution of the glycol was then added, and the solutions were mixed by bubbling air or nitrogen, or by hand. The measured reaction rate was independent of the method of mixing. The absorption–time curve was automatically recorded, at $\lambda = ca.$ 2220 Å, and was followed for a few minutes, by which time a steady " infinity " value for the absorption had been reached. An aliquot part was then removed, and its glycol concentration determined by periodate titration. Graphical methods were used for calculation of the first-order rate constants.

Although most of the work described here was on the rates of formation of the cyclic intermediates, the overall rate of oxidation was followed spectrophotometrically in a few cases. This method gave fair agreement with the chemical method (Table 4), least satisfactory with

TABLE 4. *Spectrophotometric determination of the overall rate of reaction;* pH 5·44; $I \doteq 0{\cdot}104$ (*mole l.*$^{-1}$).

Diol	[Diol] (M)	First-order rate constant (10^{-4} sec.$^{-1}$) Spectrophotometric	Chemical
Ethane-	0·0464	44·9	39·5
	0·0132	39·3	31·4
	0·00572	25·9	22·6
Propane-1 : 2-	0·045	120	107
(−)-Butane 2 : 3-	0·012	298	287
	0·030	296	295

the slower runs where effects due to ultraviolet light [6] or to the brass of the cell would be most serious. The agreement between the ratio k_t/k_b and the chemically determined equilibrium constant shows that uncertainties of this nature are not affecting the experiments on the rates of formation of the intermediates.

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[6] Head and Standing, *J.*, 1952, 1457.

920. *The Mechanism of Oxidation of α-Glycols by Periodic Acid. Part IV.* The Oxidation of 2-Methylbutane-2 : 3-diol at* pH 4·5.

By G. J. Buist and C. A. Bunton.

In the oxidation of 2-methylbutane-2 : 3-diol at pH 4·5 the cyclic intermediate is formed at a rate comparable with that of its breakdown to the products. The complex kinetic form of the oxidation can be analysed; the rates of formation of the intermediate from, and its decomposition to, the glycol and periodic acid, and the rate of decomposition to the products, are calculated.

In a kinetic study of the periodic acid oxidation of open-chain α-glycols it was found that the kinetic form could be interpreted by assuming that the reactants were in equilibrium with an intermediate, C [1a,b,2] (cf. Part III *). There were, however, certain exceptions, *e.g.*, the oxidation of pinacol, [1a,b,3] where no evidence could be found for the formation of an intermediate. Another deviation was in the oxidations of (−)-butane- and 2-methylbutane-2 : 3-diol, with glycol in excess,[4] where in the pH range 4—5 the first-order plots of log periodate *versus* time, instead of being linear, showed an initial downward curvature whose extent decreased with increasing glycol concentration (Fig. 1). This deviation from the usual simple first-order kinetics shows that there is an initial slow build-up of the intermediate. An increase in glycol concentration increases the rate of formation of the intermediate, and therefore decreases the extent of the induction period.

The kinetic form of this " non-equilibrium " system was investigated in detail for the oxidation of 2-methylbutane-2 : 3-diol at pH 4·5. A mathematical solution for reversible consecutive, first-order reactions is available.[5] Its use restricts our study to cases in which glycol is in large excess, and k_f[G] (where [G] is the concentration of glycol) is then the first-order rate constant for formation of the intermediate.

When the initial concentrations of the intermediate, C, and the products are zero, the solutions of the equation are:

$$[\mathrm{Per}]_t = \frac{[\mathrm{Per}]_0}{k(\phi_1 - \phi_2)}\left\{\phi_1(k - \phi_2)\exp(-\phi_2 t) - \phi_2(k - \phi_1)\exp(-\phi_1 t)\right\} \quad . \quad (1)$$

$$[\mathrm{C}]_t = \frac{[\mathrm{Per}]_0\phi_1\phi_2}{k(\phi_1 - \phi_2)}\left\{\exp(-\phi_2 t) - \exp(-\phi_1 t)\right\} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

and $$[\overline{\mathrm{Per}}]_t = [\mathrm{Per}]_0 - [\mathrm{Products}]_t = \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$\frac{[\mathrm{Per}]_0}{\phi_1 - \phi_2}\left\{\phi_1\exp(-\phi_2 t) - \phi_2\exp(-\phi_1 t)\right\} \quad . \quad . \quad . \quad (3a)$$

where the quantities in square brackets are the concentrations at times $t = 0$ and t, and $[\overline{\mathrm{Per}}]$ = the stoicheiometric periodate concentration, *i.e.*, $[\overline{\mathrm{Per}}] = [\mathrm{Per}] + [\mathrm{C}]$. ϕ_1 and ϕ_2 are the positive and the negative roots respectively of a quadratic equation, *i.e.*,

$$\left.\begin{matrix}\phi_1\\ \phi_2\end{matrix}\right\} = \frac{k_f[\mathrm{G}] + k_b + k \pm \sqrt{\left\{(k_f[\mathrm{G}] + k_b + k)^2 - 4kk_f[\mathrm{G}]\right\}}}{2} \quad . \quad . \quad (4)$$

Kinetic Analysis.—The rate constants k_f, k_b, and k were calculated from the experimental results by two independent methods. In the first they were calculated from the

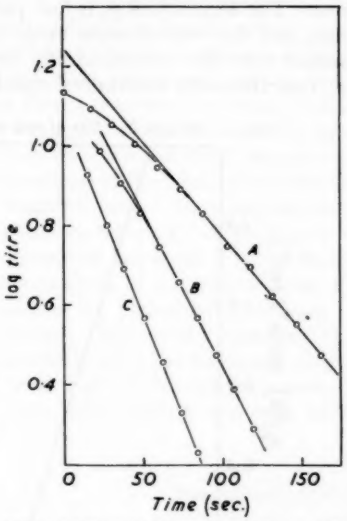
* Part III, preceding paper.

[1] Duke *et al.*, *J. Amer. Chem. Soc.*, 1947, **69**, 3054; 1954, **76**, 3803; (*b*) Buist, Bunton, and Shiner, *Research*, 1953, **6**, 45; Buist and Bunton, *J.*, 1954, 1406.
[2] Taylor, *J. Amer. Chem. Soc.*, 1953, **75**, 3912.
[3] Price *et al.*, *J. Amer. Chem. Soc.*, 1938, **60**, 2726; 1942, **64**, 552.
[4] Buist, Bunton, and Miles, *J.*, 1957, 4567.
[5] Rakowski, *Z. phys. Chem.*, 1907, **57**, 321.

values of ϕ_1 and ϕ_2, obtained from the curved first-order plot (Fig. 1). In the second, and more accurate, method they were evaluated from the variation of ϕ_2 with glycol concentration, and the limiting second-order rate constant, k_2.

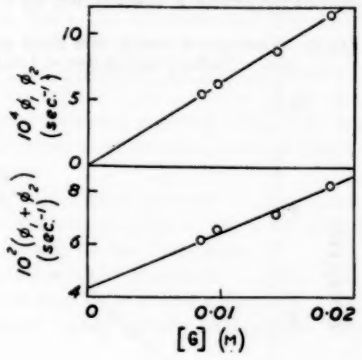
Method 1. The stoicheiometric concentration of periodate is given by the difference between the two exponential terms of equation 3*a*. The positive root ϕ_1 is greater than the negative root ϕ_2, and so the term $\phi_2 \exp(-\phi_1 t)$ decreases much more rapidly than does the term $\phi_1 \exp(-\phi_2 t)$, and soon becomes negligible. Hence the initial curvature of the " first-order plot " (Fig. 1) of log titre against time is due to the difference between these two exponential terms, but the later, linear portion is due to the term $\phi_1 \exp(-\phi_2 t)$ only.

FIG. 1. *Oxidation of* 2-*methylbutane*-2 : 3-*diol at* pH 4·5 *and* 0°.



A, [G] = 0·851 × 10^{-2}M; ϕ_2 = 106. *B*, [G] = 1·82 × 10^{-2}M; ϕ_2 = 176. *C*, [G] = 7·38 × 10^{-2}M; ϕ_2 = 228. (ϕ_2 in 10^{-4} sec.$^{-1}$.)

FIG. 2. *Method* 1. *Determination of* k, k_t, *and* k_b *from the roots* ϕ_1 *and* ϕ_2.



Values of ϕ_2 can therefore be calculated from the linear slope of the curve: this linear portion can be extrapolated back to zero time, and the equation of this straight line is:

$$\log X_t = \log\{[\text{Per}]_0/(\phi_1 - \phi_2)\}\phi_1 \exp(-\phi_2 t) \quad . \quad . \quad . \quad . \quad (5)$$

Then from equations 3 and 5, we have:

$$\log(X_t - [\overline{\text{Per}}]_t) = \log\frac{[\text{Per}]_0\phi_2}{\phi_1 - \phi_2} - \frac{\phi_1 t}{2{\cdot}3} \quad . \quad . \quad . \quad . \quad . \quad (6)$$

The quantity $X_t - [\overline{\text{Per}}]_t$ is given by the difference between the extrapolated straight portion of Fig. 1 and the experimental curve of log titre against time. Equation (6) requires that a plot of log $(X_t - [\overline{\text{Per}}]_t)$ should be linear with time. This linear relation is obeyed and the values of ϕ_1, calculated from the curved part of Fig. 1 by using equation (6), are given with values of ϕ_2, calculated from the straight portion of Fig. 1, in Table 1. (At the higher glycol concentrations, the initial curvatures are too small for ϕ_1 to be calculated.) The rate constants k_t, k_b, and k can be calculated from the relations for the roots of a quadratic:

$$\phi_1 + \phi_2 = k_t[\text{G}] + k_b + k$$

and

$$\phi_1\phi_2 = k_t k[\text{G}]$$

TABLE 1. *Analysis of the kinetics of oxidation. Method* 1.

10^3[Per]$_0$ (M)	0·76	0·69	0·68	0·98	0·64	0·68	0·94	1·03	0·94
10^3[G] [a] (M)	8·51	9·47	9·64	10·47	14·10	18·20	29·8 [b]	53·5	73·8
$10^4\phi_1$ (sec.$^{-1}$)	490	—	540	500 [c]	560	650	—	—	—
$10^4\phi_2$ (sec.$^{-1}$)	106	115	115	122	156	176	202	222	228

[a] Concentration of glycol at half reaction.
[b] This run was stopped in acid potassium iodide with consequent loss of accuracy. [c] At this, and higher, glycol concentrations the curvature was insufficient for the evaluation of ϕ_1, as can be seen by examination of the plots of log titre against time (Fig. 1).

These are shown in Fig. 2, and the values so calculated are:

$$k_1 = 2{\cdot}1 \text{ (sec.}^{-1} \text{ mole}^{-1} \text{ l.)}, \quad 10^4 k_b = 140 \text{ (sec.}^{-1}\text{)}, \quad 10^4 k = 300 \text{ (sec.}^{-1}\text{)}.$$

This method of calculation has certain limitations. The accuracy of ϕ_1 is low, particularly for runs which are complete in less than 4 min., and the concentration range of the glycol is limited to 10—20 mmole l.$^{-1}$. It is assumed that the stoicheiometric concentration of periodate is determined by titration, *i.e.*, that the value determined equals the

FIG. 3. *Variation of root ϕ_2 with glycol concentration. (Slope of broken line = $1/k_s$.)*

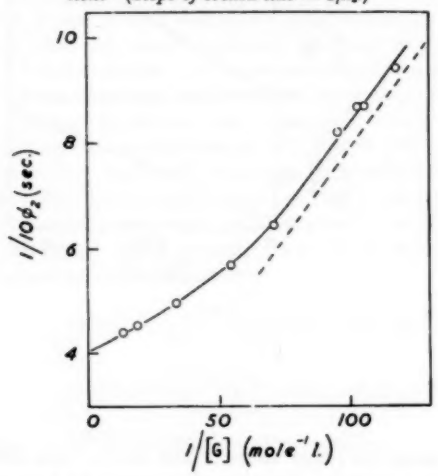
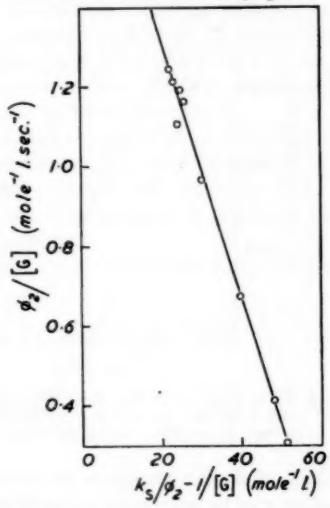


FIG. 4. *Method* 2. *Use of eqn.* 8.



sum of [Per] + [C]. Any error in this assumption will affect the curved part of Fig. 1, and hence the value of ϕ_1 (but not of ϕ_2, provided that the error is proportional). In an attempt to show that the method of stopping the run had no effect, one experiment {that with 10^3[G] = 10·47 (mole^{-1} l.), Table 1} was made in which the aliquot portions were added to acid potassium iodide, instead of to the usual stopping solution of sodium hydrogen carbonate.[1b] In this acid solution both iodate and periodate ions react with iodide ions, liberating iodine, and the accuracy is therefore limited because the titrations represent small differences in a large quantity. However, with this experimental limitation we find that the method of stopping the reaction had no effect on the results, and our assumptions on the stoicheiometry of the titrations are probably correct.

Method 2. The variation of ϕ_2 with varying concentration of 2-methylbutane-2 : 3-diol, at pH 4·5 (Table 1), is shown in Fig. 3. This is analogous to the plots of $1/k'$ against $1/[G]$,[1a,b] and the marked curvature would be expected for a reaction in which the reactants and the cyclic intermediate are not in equilibrium. From equation (4) the negative root ϕ_2 fits the quadratic:

$$\phi_2^2 - \phi_2(k_1[G] + k_b + k) + kk_1[G] = 0 \quad . \quad . \quad . \quad . \quad . \quad (7)$$

and from the definition of the limiting second-order rate constant, $k_s = kk_t/(k_b + k)$ (derived from the stationary state hypothesis), equation (7) reduces to:

$$\phi_2/[G] = k_t - \{(k_b + k)(k_s/\phi_2 - 1/[G])\} \quad . \quad . \quad . \quad . \quad . \quad (8)$$

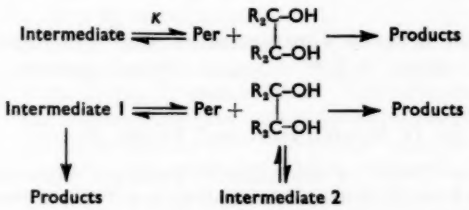
Thus a plot of $\phi_2/[G]$ against $(k_s/\phi_2 - 1/[G])$ (Fig. 4) should be linear, the slope being $-(k_b + k)$ and the intercept on the ordinate k_t, and on the abscissa $k_t(k_b + k)$. The limiting second-order rate constant k_s, and the root ϕ_2, can both be determined accurately in this system (cf. Experimental section) (and their values will not depend upon the method of stopping the reaction). We calculate the following values: $k_t = 1{\cdot}95$ (sec.$^{-1}$ mole^{-1} l.); $10^4k_b = 77$ (sec.$^{-1}$); $10^4k = 244$ (sec.$^{-1}$); and $K = k_t/k_b = 253$ (mole^{-1} l.).

These values are in fair agreement with those obtained by the simpler and less precise method 1, which depends upon analysis of the induction period of the reaction. Extrapolation of Fig. 3 to infinite glycol concentration gives a value of k, the rate constant for breakdown of the intermediate, of 247×10^{-4} (sec.$^{-1}$), in good agreement with the value obtained from the more rigorous treatment outlined above. (Such an extrapolation should give a reasonably accurate value for k even when the reactants and intermediate are not in equilibrium, although the apparent value of K will have no precise meaning.)

These methods for the determination of the rate constants for the formation and decomposition of the cyclic intermediate can only be used in certain special cases such as that described here. They supplement the spectrophotometric method (Part III), which itself can only be applied to systems in which the formation of the intermediate is not too fast to measure, but is much faster than its breakdown.

This analysis of the kinetic form enables us to distinguish between various possible mechanisms for periodate oxidations. For the oxidation of ethanediol, with glycol in large excess, Duke *et al.*[1a] observed that the reciprocal of the first-order rate constant varied linearly with the reciprocal of glycol concentration, and suggested that this proved postulated reaction through an intermediate where k_t and $k_b \gg k$, and $k_t/k_b = K$.

It was later pointed out that other mechanisms would satisfy this simple kinetic form,[2] *e.g.*:



Here the complex between glycol and periodate need not necessarily be an intermediate in the formation of the products. However, our analysis of the kinetics of oxidation of 2-methylbutane-2 : 3-diol, at pH 4·5, proves that the complex is a necessary intermediate, and that the original suggestion by Duke *et al.*[1a] is at least in some, and probably in all cases, correct.

Appendix

By using the general solution (eqns. 1, 2), we can analyse the conditions in which the kinetic form of the reaction can be used to show that the reactants and intermediate are, or are not, in equilibrium. The tests which can be used are summarised briefly as: (*a*) curvature of the plots of log [Per] *versus* time (Fig. 1), (*b*) curvature of the " reciprocal " plots,[1] and (*c*) a difference between the slope of the " reciprocal " plot and $1/k_s$. The conditions in which these tests can be used can be stated briefly as: (*a*) curvature will be observed only if ϕ_1 is not too large compared with ϕ_2; (*b*) and (*c*) if $k_t/k_b \approx 20$ the " reciprocal " plot will be linear (except for a small

part near to the intercept), with a slope $\approx 1/k_s$, even when reactants and the intermediate are not in equilibrium. If $k_1/k_b > 100$, non-attainment of equilibrium will be shown by test (*c*), although if k_1/k_b is large it may be difficult to follow the reaction in glycol concentrations low enough for the evaluation of k_s.[1a,b]

In general, lack of curvature of the plots of log [Per] *versus* time, or $1/k'$ *versus* 1/[G], cannot be taken as proof of attainment of equilibrium between reactants and the cyclic intermediate. Agreement between the slope of the " reciprocal " plot and $1/k_s$ (test *c*) is a much more useful criterion, but this can fail in certain cases, and the only rigorous and general methods are those physical methods (*e.g.*, spectral or pH changes) which give direct evidence about the rate of formation of the cyclic intermediate.

Experimental

The materials were prepared, and the reactions followed, by the procedures outlined in earlier papers. All reactions were followed in water, at 0°, at pH 4·5 and ionic strength = 0·021 mole^{-1} l.

The data on which the limiting second-order rate constant, k_s is evaluated are as in Table 2.

Table 2.

Initial concns. (10^{-4}M)		Second-order rate constant k'' (sec.$^{-1}$ mole^{-1} l.)
[Per]	[G]	
13·33	23·37	1·48
10·25	6·38	1·46
6·17	3·94	1·50
3·00	3·28	1·46

i.e., k_s = 1·48 (sec.$^{-1}$ mole^{-1} l.).

William Ramsay and Ralph Forster Laboratories, University College, Gower Street, London, W.C.1. [*Received, May 6th*, 1957.]

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921. *The Relation between Configuration and Conjugation in Diphenyl Derivatives. Part IX.* Some Tetrachloro-2 : 2′-bridged Compounds.*

By D. Muriel Hall and Fatima Minhaj.

A series of 4 : 6 : 4′ : 6′-tetrachloro-2 : 2′-bridged diphenyls has been prepared from 4 : 6 : 4′ : 6′-tetrachlorodiphenic acid. The ultraviolet absorption spectra of these compounds show increased intensities and red shifts of the conjugation band, in comparison with the corresponding unsubstituted compounds, in spite of the presence of the large chlorine atoms in the *ortho*-positions. In contrast, the conjugation band in 2 : 4 : 2′ : 4′-tetrachlorodiphenyl is present only as an inflection at a shorter wavelength.

These results emphasise the importance of a 2 : 2′-bridge in maintaining conjugation in *ortho*-substituted diphenyls.

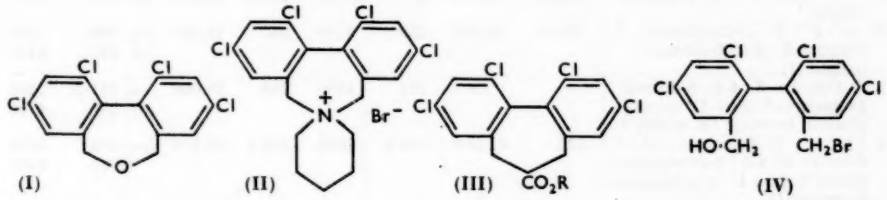
Spectroscopic measurements show that 2 : 2′-bridged diphenyls in which the bridge forms part of a homocyclic or heterocyclic 7-membered ring retain a high degree of conjugation between the two benzene rings.[1,2,3] Investigation of the effect of *ortho*-substituents on the spectra of these compounds has been restricted to compounds with heterocyclic

* Part VIII, *J.*, 1957, 651.

[1] Beaven, Hall, Lesslie, and Turner, *J.*, 1952, 854.
[2] Beaven, Bird, Hall, Johnson, Ladbury, Lesslie, and Turner, *J.*, 1955, 2708.
[3] Beaven and Johnson, *J.*, 1957, 651.

bridging rings and to the substituents methoxyl [1] and methyl.[4] It thus seemed desirable to extend this range by investigating the effect of chlorine atoms in the *ortho*-positions on the ultraviolet absorption spectra of such bridged compounds. For this, 6 : 6′-dichlorodiphenic acid [5] was required as starting material. However, in view of the much shorter synthesis of 4 : 6 : 4′ : 6′-tetrachlorodiphenic acid [6] (in two stages from anthranilic acid), the latter compound was preferred and, accordingly, a series of tetrachloro bridged compounds was prepared.

Methyl 4 : 6 : 4′ : 6′-tetrachlorodiphenate was reduced with lithium aluminium hydride and the resulting diol dehydrated to give the oxepin (I). A solution of the diol in glacial acetic acid was treated with hot hydrobromic acid and gave a dibromide which was a gum. The azepinium bromide (II) was prepared by the condensation of piperidine with the dibromide; the reaction of the latter with sodiomalonic ester gave a cyclic ester from which,



after suitable treatment, methyl 2′ : 4′ : 1″ : 3″-tetrachloro-3 : 4-5 : 6-dibenzo*cyclo*hepta-3 : 5-diene-1-carboxylate (III; R = Me) was obtained. Treatment of the dibromide with the sodio-derivative of ethyl ethane-1 : 1 : 2 : 2-tetracarboxylate failed to give any of the ester with an eight-membered ring and 71% of the original ester was recovered (cf. the corresponding reaction with 2 : 2′-bisbromomethyldiphenyl [2]). On the other hand, reaction between the dibromide and ethyl propane-1 : 1 : 3 : 3-tetracarboxylate in the presence of sodium ethoxide led, as with 2 : 2′-bisbromomethyldiphenyl, to fission of the carbon chain of the ester and the formation of the compound with a 7-membered ring, from which the acid (III; R = H) was obtained.

From all these condensations of the dibromide with esters in the presence of sodium ethoxide appreciable quantities (sometimes as much as 40%, based on the diol used to prepare the dibromide) of the oxepin (I) were isolated. This suggested that the dibromide was contaminated with the bromohydrin (IV), which would readily form the oxepin in the presence of alkali, and, indeed, by heating this " dibromide " (*i.e.*, the gum as used for the above condensations) for about 10 min. with 30% sodium hydroxide, oxepin was obtained. Subsequently, by prolonged boiling of the diol with a larger excess of hydrobromic acid and no acetic acid, the dibromide was obtained as a crystalline solid. Unlike the gum, this was unaffected when heated with 30% sodium hydroxide for 10 min.

Discussion of Spectra.—The ultraviolet absorption spectra (Figs. 1 and 2) of the compounds (I), (II), and (III) show long-wave shifts and increased intensities of the conjugation band, as compared with the corresponding unsubstituted compounds (Table 1). Similar effects are apparent in the long-wave fine structure (which is rather more highly developed in the tetrachloro-compounds), in the minimum on the short-wave side of the conjugation band, and, where data are available, in the shortwave band itself, although here the increases in intensity are proportionately rather small and may hardly be significant.

Introduction of the four chlorine atoms into these bridged compounds clearly does not reduce the conjugation between the benzene rings and, while the *ortho*-chlorine atoms may

[4] Wittig and Zimmermann, *Chem. Ber.*, 1953, **86**, 629.
[5] Christie, James, and Kenner, *J.*, 1923, **123**, 1948.
[6] Atkinson, Murphy, and Lufkin, *Org. Synth.*, 1951, **31**, 96.

reduce somewhat the auxochromic influence which the *para*-chlorine atoms would otherwise have, their steric effect on conjugation is nevertheless slight. This is in accordance with our view that fairly large substituents can be accommodated in the *ortho*-positions of 2 : 2′-bridged diphenyls with only slight distortion of the bridging ring, since the angle θ between the planes of the benzene rings is already, in the unsubstituted compounds, of the order of 45—50°. Further, the *ortho*-substituents can undoubtedly approach one another more closely when free rotation of the benzene rings is prevented by bridging than they can

TABLE 1. *Ultraviolet absorption spectra of 2 : 2′-bridged diphenyls.*

	Short-wave band		Minimum		Conjugation band		Long-wave features	
Compound	$\lambda_{max.}$	$\varepsilon_{max.}$	$\lambda_{min.}$	$\varepsilon_{min.}$	$\lambda_{max.}$	$\varepsilon_{max.}$	$\lambda_{max.}$	$\varepsilon_{max.}$
2 : 7-Dihydro-3 : 4-5 : 6-dibenzoxepin [3]	206·5	40,000	227	4920	250·5	16,500	(*ca.* 277)	1600
2′ : 4′ : 1″ : 3″-Tetrachloro-2 : 7-dihydro-3 : 4-5 : 6-dibenzoxepin (I)	217·5	42,500	239	9500	257	19,000	(*ca.* 290) (*ca.* 280)	1200 3400
2 : 7-Dihydro-3 : 4-5 : 6-dibenzazepinium-1-*spiro*-1‴-piperidinium bromide (in water) [1]	—	—	224	4500	248	15,000	(*ca.* 281·5) (*ca.* 272)	2250 4750
2′ : 4′ : 1″ : 3″-Tetrachloro-2 : 7-dihydro-3 : 4-5 : 6-dibenzazepinium-1-*spiro*-1‴-piperidinium bromide (II)	222	41,500	242·5	9600	259·5	18,100	(*ca.* 293) 283·5	3550 6520
Methyl 3 : 4-5 : 6-dibenzo*cyclo*hepta-3 : 5-diene-1-carboxylate [2]	207·5	42,500	227·5	5700	248·5	15,500	(*ca.* 274)	1700
Methyl 2′ : 4′ : 1″ : 3″-tetrachloro-3 : 4-5 : 6-dibenzo*cyclo*hepta-3 : 5-diene-1-carboxylate (III)	215·5 (*ca.* 223)	46,000 41,500	236	8400	254·4	19,000	(*ca.* 286)	810

Solvent, 96% ethanol, except where otherwise stated; wavelengths in mμ; values in parentheses denote inflections.

in a non-bridged compound, where interactions between such *ortho*-substituents are probably the dominant factor in determining preferred conformation. (For small *ortho*-substituents, therefore, such distortion of the bridging ring is probably negligible.) Calculations of θ with use of normal covalent radii and bond angles give values of 43°, 47° *, and 49° for the unsubstituted oxepin, azepinium bromide, and dibenzo*cyclo*heptadiene, respectively. The angles measured on our (rigid) molecular models have similar values since the models incorporate the same bond lengths and angles. It is less easy to predict the amount of distortion permitted, and here the use of highly flexible models may give misleading results. Braude and Forbes,[7] using " open " scale models, find θ to be about 21° in the unsubstituted oxepin but their model, shown in a photograph, appears to be considerably distorted so that the two benzene rings are no longer collinear.

These authors regard 2 : 2′-bridged diphenyls as compounds which manifest steric effects predominantly by changes in the absorption intensity and not by wavelength displacements. For such compounds they calculate [8] the approximate mean interplanar angle θ from the expression $\cos^2\theta = \varepsilon/\varepsilon_0$, where ε is the molecular extinction coefficient for the diphenyl band in the particular compounds and ε_0 is the corresponding value for fluorene, which they regard as a planar, *oo*′-disubstituted diphenyl.

Since the two rings in fluorene are planar but not collinear [9] the molecule must be

* The C–N^+ bond length is taken as 1·50 Å.

[7] Braude and Forbes, *J.*, 1955, 3776.
[8] Braude, *Experientia*, 1955, **11**, 457; Braude and Sondheimer, *J.*, 1955, 3754.
[9] Brown and Bortner, *Acta Cryst.*, 1954, **7**, 139; Burns and Iball, *Nature*, 1954, **173**, 635; *Proc. Roy. Soc.*, 1955, *A*, **227**, 200.

somewhat strained and so appears to be rather unsuitable as a standard. A more serious objection, however, to the validity of such calculations of θ is that the intensity and, to a smaller degree, the position of the diphenyl hand in these bridged compounds are affected by the presence (and nature) of substituents in the *para-*, *meta-*, or *ortho*-positions; in the last case a steric effect may be superimposed. These points are illustrated by some of the compounds quoted by Braude and Forbes. (1) *N*-Acetylcolchinol methyl ether (V) has $\varepsilon_{max.}$ 20,000 at 262 mμ,[10] from which Braude and Forbes calculate θ to be zero. However the increased intensity of absorption is almost certainly due to the presence of *pp'*-methoxyl groups, which here more than compensate for the effects of the single *o*- and *m*-methoxyl groups. Additional evidence for the non-planarity of a diphenyl with a three-carbon bridge comes from the preparation by Iffland and Siegel [11] of ethyl 3 : 4-5 : 6-dibenzo*cyclo*hepta-3 : 5-diene-1 : 1-dicarboxylate (VI) in an optically active form, although, of course, the existence of optical isomerism in a compound of this type gives no direct

FIG. 1. FIG. 2. FIG. 3.

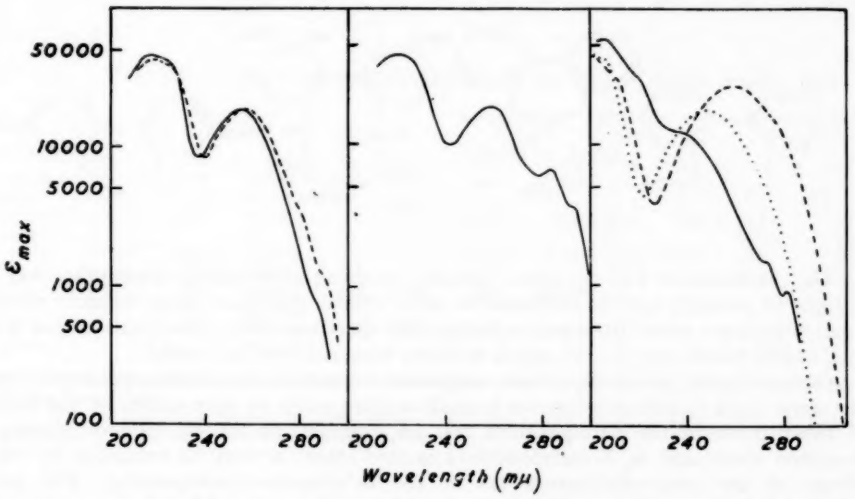


FIG. 1. ——— Methyl 2′ : 4′ : 1″ : 3″-tetrachloro-3 : 4-5 : 6-dibenzo*cyclo*hepta-3 : 5-diene-1-carboxylate (III; R = Me). – – – – 2′ : 4′ : 1″ : 3″-Tetrachloro-2 : 7-dihydro-3 : 4-5 : 6-dibenzoxepin (I).

FIG. 2. 2′ : 4′ : 1″ : 3″-Tetrachloro-2 : 7-dihydro-3 : 4-5 : 6-dibenzazepinium-1-*spiro*-1‴-piperidinium bromide (II).

FIG. 3. ——— 2 : 4 : 2′ : 4′-Tetrachlorodiphenyl. – – – – 4 : 4′-Dichlorodiphenyl. ..... Diphenyl

indication of the value of θ except that it must be greater than zero. (2) The *oo'*-dimethoxy-derivatives [1] of 9 : 10-dihydrophenanthrene and 2 : 7-dihydro-3 : 4-5 : 6-dibenzoxepin show a larger reduction in intensity of the conjugation band than do the corresponding *oo'*-dimethyl derivatives,[4] * although methyl causes much greater steric interference than

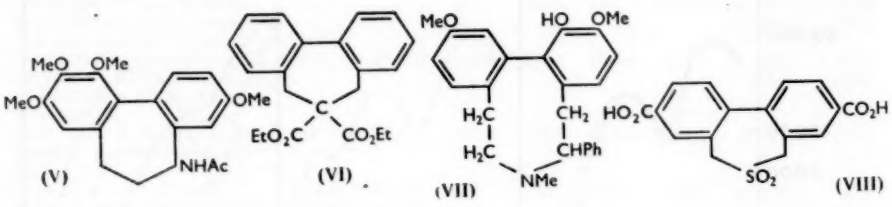
* Bergmann and Pelchowicz [12] have also determined the spectrum of 9 : 10-dihydro-4 : 5-dimethylphenanthrene but their data in the text are at variance with their drawing of the spectrum and we have therefore only considered Wittig and Zimmermann's figures.

[10] Huang, Tarbell, and Arnstein, *J. Amer. Chem. Soc.*, 1948, **70**, 4181; Horowitz, Ullyot, E. C. Horning, M. G. Horning, Koo, Fish, Parker, and Walker, *ibid.*, 1950, **72**, 4330; Rapoport, Williams, and Cisney, *ibid.*, 1951, **73**, 1414.

[11] Iffland and Siegel, *J. Org. Chem.*, 1956, **21**, 1056.

[12] Bergmann and Pelchowicz, *J. Amer. Chem. Soc.*, 1953, **75**, 2663.

methoxyl (in which the methyl group can be out of the way). (3) In a compound with a large 2 : 2′-bridge as in dihydrophenylthebaine (VII) the molecule is more flexible and a number of conformations are possible. From our models it appears that θ cannot be less than about 50° but could be as large as 110°. Preferred conformations, of which there may be several, probably have intermediate values of θ. It is therefore not surprising that the conjugation band is apparently absent,[13] although evidence from compounds with a four-carbon bridge [2,14] suggests that it might be detectable, at least as an inflection, at a much shorter wavelength. The band at 281 mμ ($\varepsilon_{max.}$ 5600) in dihydrophenylthebaine cannot be a diphenyl band at all and is presumably the normal long-wave band due to absorption by methoxyphenyl partial chromophores. (4) The effect of *meta*-substituents is attributed by Braude and Forbes to " buttressing " of the *o*-hydrogen atoms against in-plane bending away from the diphenyl link. However, on their hypothesis, the steric effect of such " buttressed " hydrogen atoms (in the *mm*′-dimethoxy-compounds) on the spectrum of, for example, the oxepin [15] ($\varepsilon_{max.}$ 11,000) would be as great as that of two *ortho*-methyl groups [4] ($\varepsilon_{max.}$ 11,000).



The calculation of θ by the above formula, involving as it does the assumption that *all* changes in intensity may be attributed to steric effects, thus leads to inconsistent results. Further evidence comes from our work, since the spectrum of the tetrachloro-oxepin, with $\varepsilon_{max.}$ 19,000, would give θ = 0°, which is clearly impossible on any model.

Our view is still that in the oxepins, azepinium compounds, and dibenzo*cyclo*heptadienes the steric effect of *ortho*-substituents is small and can easily be over-ridden by the effects of substituents in the *para*-positions (as, for example, in the tetrachloro-compounds described above and in *N*-acetylcolchinol methyl ether) or may be enhanced by other effects of the *ortho*-substituents (as in the *oo*′-dimethoxy-compounds). The large mesomeric effect of methoxyl groups makes them rather unsuitable substituents for the study of steric effects, and a series of other *oo*′-disubstituted bridged diphenyls is in preparation. Qualitatively, the 9 : 10-dihydrophenanthrenes behave in the same way as the compounds with larger bridging rings but in view of the smaller value of θ (15—16°, depending on the length of the central diphenyl bond) it is likely that *large ortho*-substituents, which can readily be accommodated when θ is about 50°, will cause appreciable molecular distortion here. Even so, this is not *necessarily* accompanied by much loss of conjugation but further experimental evidence is required.

Truce and Emrick [16] correlate the position of the conjugation band in seven-membered ring bridged diphenyls with optical stability and suggest that $\lambda_{max.}$ 242 mμ " represents about the borderline in resolvability "; compounds with the band at longer wavelengths would either not be resolvable or would be optically unstable. There is independent evidence from other work [17] that increase in θ leads to increase in optical stability but,

[13] Small, Sargent, and Bralley, *J. Org. Chem.*, 1947, **12**, 839.
[14] Cope and Smith, *J. Amer. Chem. Soc.*, 1956, **78**, 1012.
[15] Beaven, Hall, Lesslie, Turner, and Bird, *J.*, 1954, 131.
[16] Truce and Emrick *J. Amer. Chem. Soc.*, 1956, **78**, 6130.
[17] Hall and Turner, *J.*, 1955, 1242; Hall, *J.*, 1956, **3674**; Armarego and Turner, *J.*, 1956, 3668; 1957, 13.

while it appears probable that in the absence of all other substituents the position of the conjugation band may be roughly correlated with the value of θ, it cannot be expected that small variations in $\lambda_{max.}$ will be reflected in racemisation rates. Among seven-membered ring bridged diphenyls *without ortho*-substituents optical activity has been demonstrated only in ethyl 3 : 4-5 : 6-dibenzo*cyclo*hepta-3 : 5-diene-1 : 1-dicarboxylate [11] (VI) and 2 : 7-dihydro-3 : 4-5 : 6-dibenzothiepin-2′ : 3″-dicarboxylic acid 1 : 1-dioxide (VIII).[16] The former racemises in about 5 hr. at 32·5° but no information is available about the optical stability of the latter. (Incidentally we find 3 : 4-5 : 6-dibenzo*cyclo*hepta-3 : 5-diene-1 : 1-dicarboxylic acid to have $\varepsilon_{max.}$ 15,000 at 250 mμ, not *ca.* 100,000 as described by Truce and Emrick.)

In contrast to the bridged compounds, unbridged diphenyls are far more sensitive spectroscopically to the presence of *ortho*-substituents. For comparison with the bridged compounds it was desirable to examine 2 : 4 : 2′ : 4′-tetrachlorodiphenyl. This compound proved unexpectedly difficult to prepare. It is described by Ullmann [18] as a solid, m. p. 83°, obtained by heating 2 : 4-dichloro-1-iodobenzene with copper bronze. The only other reference to it describes its isolation [19] from the products of thermal decomposition

TABLE 2. *Ultraviolet absorption spectra of non-bridged diphenyls.*

	Short-wave band		Minimum		Conjugation band		Minimum		Long-wave band	
Compound	$\lambda_{max.}$	$\varepsilon_{max.}$	$\lambda_{min.}$	$\varepsilon_{min.}$	$\lambda_{max.}$	$\varepsilon_{max.}$	$\lambda_{min.}$	$\varepsilon_{min.}$	$\lambda_{max.}$	$\varepsilon_{max.}$
Diphenyl [a]	203	46,000 [b]	222	4300	249	17,300	—	—	—	—
	(*ca.* 205)	42,000 [b]								
2 : 2′-Dichlorodiphenyl [c]	208	36,000	—	—	(230)	6600	264	700	273·5	540
									266·5	735
2 : 4 : 2′ : 4′-Tetrachlorodiphenyl	205·5	55,000	—	—	(*ca.* 237)	12,300	271·5	1445	281	900
	(*ca.* 221)	28,000							272	1450
4-Chlorodiphenyl [d]	203	40,500	225	3700	253	21,100	—	—	—	—
	(210)	(32,000)								
4 : 4′-Dichlorodiphenyl	201	42,400	226	3810	259	25,200	—	—	(*ca.* 283)	9000
	(*ca.* 211)	29,100							(*ca.* 275)	16,000

Solvent, 96% ethanol, except where otherwise stated; wavelengths in mμ; values in parentheses denote inflections.
[a] Everitt, Hall, and Turner, *J.*, 1956, 2286. [b] In light petroleum (b. p. 100—120°). [c] Beaven and Hall, *J.*, 1956, 4637. [d] G. H. Beaven, personal communication.

of 2 : 4 : 2′ : 4′-tetrachlorodibenzoyl peroxide. We failed to prepare it either by Ullmann's method (including considerable variation in the temperature of the reaction) or by the diazo-process (Sandmeyer or Gattermann) from 2 : 2′-dichlorobenzidine.[20] It was finally obtained as a solid, m. p. 41°, in 13% yield by the action of anhydrous cupric chloride on 2 : 4-dichlorophenylmagnesium iodide (Krizewsky–Turner method [21]). Possibly this is a metastable form, but the m. p. has remained unchanged for several months.

Its spectrum (Fig. 3) shows greater conjugation than that of 2 : 2′-dichlorodiphenyl,[22] as evidenced by long-wave shifts and increased intensities, but the compound is nevertheless very much *less* conjugated than the parent diphenyl (Table 2), the conjugation band being present only as an inflection ($\lambda_{infl.}$ *ca.* 236 mμ) The results for 4-chloro- and 4 : 4′-dichloro-diphenyl show the auxochromic effects of *para*-chlorine atoms on the diphenyl chromophore (Table 2; Fig. 3).

[18] Ullmann, *Annalen*, 1904, **332**, 38.
[19] Fichter and Adler, *Helv. Chim. Acta*, 1926, **9**, 279.
[20] Cain and May, *J.*, 1910, **97**, 720.
[21] Krizewsky and Turner, *J.*, 1919, **115**, 559; Turner, *J. Proc. Roy. Soc. New South Wales*, 1920, **54**, 37.
[22] Beaven and Hall, *J.*, 1956, 4637.

Experimental

Methyl 4 : 6 : 4′ : 6′-*Tetrachlorodiphenate*.—4 : 6 : 4′ : 6′-Tetrachlorodiphenic acid,[6] m. p. 264—265°, was heated under reflux with its own weight of concentrated sulphuric acid and 10 times its weight of methanol for 18 hr. Prolonged heating was necessary to complete esterification of both carboxyl groups. The *dimethyl ester*, crystallised from methanol or benzene, had m. p. 160—161° (Found: C, 47·0; H, 3·1; Cl, 35·2. $C_{16}H_{10}O_4Cl_4$ requires C, 47·1; H, 2·5; Cl, 34·8%). The *diamide* was prepared *via* the acid chloride and had m. p. 246—247° (from $CHCl_3$) (Found: C, 44·4; H, 1·9; N, 7·6; Cl, 37·8. $C_{14}H_8O_2N_2Cl_4$ requires C, 44·5; H, 2·1; N, 7·4; Cl, 37·5%).

4 : 6 : 4′ : 6′-*Tetrachloro*-2 : 2′-*bishydroxymethyldiphenyl*.—The above ester was reduced with lithium aluminium hydride in ether, the finely-ground solid ester being washed into the reaction flask with ether. The mixture was heated (water-bath) for 40 min., then decomposed with water and 2N-sulphuric acid. The ethereal layer was separated, the ether removed, and the residue crystallised from carbon tetrachloride, giving the *diol* (98%) as needles, m. p. 136—137° (Found: C, 47·8; H, 2·9; Cl, 40·6. $C_{14}H_{10}O_2Cl_4$ requires C, 47·8; H, 2·9; Cl, 40·3%).

2′ : 4′ : 1″ : 3″-*Tetrachloro*-2 : 7-*dihydro*-3 : 4-5 : 6-*dibenzoxepin* (I) was obtained by heating the above diol (1 g.) with 50% sulphuric acid (20 c.c.) for about ½ hr. with frequent stirring. It crystallised from methanol in long, pointed prisms, m. p. 151—152·5° (Found: C, 50·3; H, 2·5; Cl, 42·2. $C_{14}H_8OCl_4$ requires C, 50·3; H, 2·4; Cl, 42·5%).

2 : 2′-*Bisbromomethyl*-4 : 6 : 4′ : 6′-*tetrachlorodiphenyl*.—(*a*) The above diol (35·2 g.) was dissolved in hot glacial acetic acid (110 c.c.) and heated with hydrobromic acid (500 c.c., 48%) under reflux for 2½ hr. The mixture was allowed to cool and the acids were decanted from the residual gum. This was dried *in vacuo* over potassium hydroxide for 48 hr., dissolved in ether, and used immediately for condensations with the esters.

(*b*) The diol (5 g.) was dissolved in hot glacial acetic acid (20 c.c.) and heated with hydrobromic acid (150 c.c., 48%) under reflux for 2½ hr. The mixture was allowed to cool, the supernatant liquid discarded, and the residual gum washed with cold water and dissolved in benzene. The benzene solution was then washed with aqueous sodium hydrogen carbonate and with water, and was used for the condensation with piperidine.

(*c*) The diol (7·5 g.) was heated with hydrobromic acid (225 c.c.) under reflux for 2½ hr. More acid (225 c.c.) was added and heating continued for a further 5 hr. The acid was decanted and the remaining oil heated with fresh acid (225 c.c.) for 2 hr. The product was washed with water, dried, and crystallised from light petroleum (b. p. 40—60°), giving 7·5 g. (74%) of the *dibromide*. After recrystallisation from ethanol it had m. p. 101·5—103·5° (Found: C, 34·8; H, 1·6; Hal, 62·3. $C_{14}H_8Br_2Cl_4$ requires C, 35·2; H, 1·7; Hal, 63·1%).

2′ : 4′ : 1″ : 3″-*Tetrachloro*-2 : 7-*dihydro*-3 : 4-5 : 6-*dibenzazepinium*-1-spiro-1‴-*piperidinium Bromide* (II).—The above dibromide, freshly prepared from the diol (5 g.) by method (*b*), was dissolved in benzene, and piperidine (2 g.) in benzene added. A flocculent precipitate, m. p. 141—143° (decomp.) (5·5 g.), separated on warming; after two crystallisations from water the *azepinium bromide* was obtained as a dihydrate, m. p. *ca.* 211—212° (Found: C, 43·7; H, 4·1; Br, 15·4; H_2O, 6·5. $C_{19}H_{18}NBrCl_4,2H_2O$ requires C, 44·0; H, 4·3; Br, 15·4; H_2O, 6·95%). Most of the water of crystallisation was readily lost *in vacuo*; the resulting bromide was extremely hygroscopic. The spectrum was determined on the air-dried dihydrate.

2′ : 4′ : 1″ : 3″-*Tetrachloro*-3 : 4-5 : 6-*dibenzo*cyclo*hepta*-3 : 5-*diene*-1 : 1-*dicarboxylic Acid*.—Sodium (4·6 g.) was dissolved in absolute ethanol (110 c.c.) and ethyl malonate (15 g.) added with stirring. An ethereal solution (300 c.c.) of the dibromide [from 35·2 g. of diol by method (*a*)] was added and the mixture heated for 40 min. Most of the ether was removed by distillation and the reaction mixture then heated under reflux with stirring for 2½ hr. Water was added and a wax separated. This was crystallised from ethanol and then heated under reflux with alcoholic potassium hydroxide. An alkali-insoluble solid was obtained which, after crystallisation from methanol, had m. p. and ultraviolet absorption spectrum identical with those for the oxepin (yield 13·9 g., 42%). Acidification of the alkaline solution, followed by ether-extraction and removal of solvent, gave the *dicarboxylic acid*, m. p. 172—175° (decomp.) (yield 9·5 g., 23%). After crystallisation from aqueous alcohol it had m. p. 188—189° (decomp.) (Found: C, 48·8; H, 2·4; Cl, 34·0. $C_{17}H_{10}O_4Cl_4$ requires C, 48·6; H, 2·4; Cl, 33·8%). From one preparation the pure *diethyl ester*, m. p. 140—141°, was isolated (Found: C, 52·9; H, 3·0; Cl, 29·8. $C_{21}H_{18}O_4Cl_4$ requires C, 53·0; H, 3·8; Cl, 29·8%).

2′ : 4′ : 1″ : 3″-Tetrachloro-3 : 4-5 : 6-dibenzocyclohepta-3 : 5-diene-1-carboxylic acid (III; R = H) was obtained by heating the dicarboxylic acid in a bath at *ca.* 200° until evolution of carbon dioxide ceased. It crystallised from ethanol in needles or plates, m. p. 219—221° (Found: C, 51·5; H, 2·8; Cl, 37·3. $C_{16}H_{10}O_2Cl_4$ requires C, 51·1; H, 2·7; Cl, 37·7%). The *methyl ester* crystallised from methanol in needles, m. p. 159—160° (Found: C, 52·7; H, 3·2; Cl, 36·1. $C_{17}H_{12}O_2Cl_4$ requires C, 52·3; H, 3·1; Cl, 36·4%).

Attempted Condensation of the Dibromide with Ethyl Ethane-1 : 1 : 2 : 2-tetracarboxylate.—Sodium (3·1 g.) was dissolved in absolute ethanol (45 c.c.) and powdered ethyl ethane-1 : 1 : 2 : 2-tetracarboxylate (21·2 g.) added with stirring, followed by the dibromide [prepared from 23·5 g. of diol by method (*a*)] in ethereal solution. The mixture was heated under reflux for ½ hr. Most of the ether was distilled off and heating continued for another 2 hr. Water was added and the wax obtained was crystallised from *n*-hexane and then from ethanol, giving ethyl ethane-1 : 1 : 2 : 2-tetracarboxylate, m. p. and mixed m. p. 73—75° (15 g., 71%), and the oxepin, m. p. 151—152° (7 g., 31%). No other product was detected.

Attempted Condensation of the Dibromide with Ethyl Propane-1 : 1 : 3 : 3-tetracarboxylate.—Similar condensation of the dibromide (from 23·5 g. of diol) with ethyl propane-1 : 1 : 3 : 3-tetracarboxylate (22·1 g.) in the presence of sodium ethoxide (from 3·1 g. of sodium) gave a solid which was heated with aqueous potassium hydroxide for 12 hr. The product was separated into oxepin, m. p. 149—150° after crystallisation (4·4 g., 20%), and a mixture of di- and mono-carboxylic acids (partial decarboxylation having occurred). The acids were heated to complete decarboxylation and the resulting 2′ : 4′ : 1″ : 3″-tetrachloro-3 : 4-5 : 6-dibenzo*cyclo*hepta-3 : 5-diene-1-carboxylic acid crystallised from benzene: m. p. and mixed m. p. 218—219° (4·8 g., 19%).

2 : 4 : 2′ : 4′-Tetrachlorodiphenyl.—Anhydrous cupric chloride (67 g., 1·25 mol.) was added gradually to a Grignard reagent prepared from 2 : 4-dichloro-1-iodobenzene [18] (109 g., 1 mol.) and magnesium (9·7 g.) in ether. The mixture was heated under reflux for 2 hr., then poured into water, and the whole acidified and filtered through a pad of kieselguhr. The ethereal layer was separated, washed with brine, and dried. After removal of the ether the residue was distilled under reduced pressure; *m*-dichlorobenzene and unchanged 2 : 4-dichloro-1-iodobenzene came over first, followed by an oil which, after redistillation, had b. p. 146°/2 mm. and solidified on treatment with ethanol. It was crystallised from ethanol and had m. p. 41—42° (Found: Cl, 48·4. $C_{12}H_6Cl_4$ requires Cl, 48·6%) (yield 7·8 g., 13%).

Absorption spectra were measured on a Unicam S.P. 500 photoelectric spectrophotometer. Inflections were confirmed photographically by Dr. G. H. Beaven by the logarithmic-cam, moving-plate method [23] but the wavelengths given in the Tables for the inflections are those obtained by direct examination of large-scale plots.

We thank Dr. G. H. Beaven for helpful discussions and for checking inflections in the spectra. We also thank the Council of Bedford College for a Postgraduate Studentship (to F. M.), the University of Aligarh for study leave (to F. M.), and the Central Research Funds Committee of the University of London for a grant (to D. M. H.) for the purchase of a spectrophotometer.

BEDFORD COLLEGE, UNIVERSITY OF LONDON. [*Received, June 11th*, 1957.]

[23] Holiday, *J. Sci. Instr.*, 1937, **14**, 166.

922. *Induction Effects in the Oxidation of Bisulphite Ion at* pH 4.

By G. A. Bottomley and W. R. Cullen.

The rate of oxygen absorption by bisulphite solutions at pH 4 in the presence of Cu^{2+} and Mn^{2+} has been studied with emphasis on the phenomena occurring when the oxygen supply is temporarily withdrawn. The absorption of oxygen after interruption follows a different course from that of an uninterrupted reaction and is most satisfactorily explained by a slow reaction of the metal catalyst with the sulphite solution.

Aqueous solutions of potassium metabisulphite (pyrosulphite) (0·10M-$K_2S_2O_5$) in potassium hydrogen phthalate buffer (0·2M) were mechanically shaken with oxygen at 25°, and the volume of oxygen absorbed determined as a function of time. Oxidation proceeds to HSO_4^-, with 1—2% at most of $S_2O_6^{2-}$. As with the extensively investigated oxidation of SO_3^{2-} at pH 8—11 the system is highly sensitive to traces of catalysts such as Cu^{2+} and to inhibitors, but at pH 4 the rate is comparatively low. No extended effort was made to work with pure solutions; instead, catalysts have been deliberately added.

Experimental

Materials.—" AnalaR " potassium metabisulphite and potassium hydrogen phthalate were twice recrystallised; the water used was prepared as for conductivity purposes and finally distilled from a silica still. Other chemicals were " AnalaR." The oxygen, normally stored over distilled water, was either prepared by the action of heat on " AnalaR " potassium permanganate and circulation over moist potassium hydroxide pellets to remove carbon dioxide, with dust filters to remove dust or manganese compounds, or obtained from a cylinder and passed slowly over platinised asbestos at 800° to oxidise possible traces of organic compounds. No difference could be detected between the samples.

Apparatus.—The absorption apparatus was a flask of 110 ml. capacity fitted with two B16 standard conical joints, one serving as a stopper through which reagents were introduced, and the other leading *via* a flexible glass tube to a 50 ml. constant-pressure absorption burette with mercury as the confining liquid. Both joints remained essentially gas-tight for an indefinite period when lubricated with a few drops of water and firmly assembled. The absorption flask was shaken by a reciprocating action through about 1 in. at a maximum rate of 400 times per min. in a thermostat at 25°. The burette was kept at the same temperature by a water jacket through which circulated water from the thermostat. The oxygen and water supplies were stored in all-Pyrex apparatus to eliminate possible inhibitors from rubber connections.

A three-way tap between the burette and the absorption flask enabled the flask to be purged with oxygen, the burette to be refilled in a few seconds, or cylinder nitrogen, cylinder carbon dioxide, and vacuum connections to be used.

Method.—The reaction flask was cleaned briefly with " chromic acid," steamed for an hour, and throughly rinsed with distilled water before each run. The necessary buffer solution was added, and the flask positioned in the shaker and left for 30 min. to come to temperature equilibrium. Then the required amount of solid metabisulphite was dropped into the buffer, the flexible lead attached, and the air displaced with oxygen. Finally the oxygen-filled burette was connected to the flask. The experiment was started by switching on the shaker and continued by taking readings of the volume absorbed at suitable time intervals. Virtually no oxidation takes place before shaking begins because little metabisulphite dissolves unassisted and the rate of reaction with unshaken solutions is very low. Tests with alkaline pyrogallol showed that the uptake of oxygen was five times that of the highest obtained with sulphite so that we were confident that oxygen diffusion into the solution was never a limiting factor. Reagents were introduced when required through the standard joint-stopper arm during a momentary cessation of the shaking.

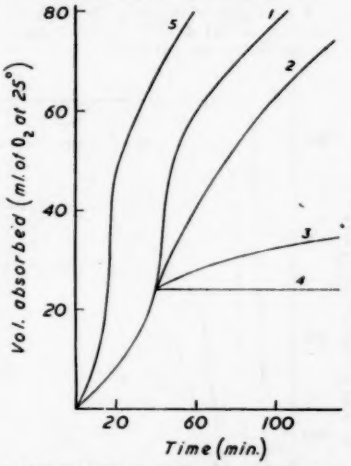
Results.—The results are shown in Figs. 1—5. In each experiment it was usual to take

volume readings at intervals of 1 min. for the first hour and then at longer intervals. The experimental points did not deviate from the smooth lines shown by more than 0·5 ml.

Curve 1, Fig. 1, shows the absorption–time curve for 75 ml. of a solution of 0·10M-potassium metabisulphite and 0·2M-potassium hydrogen phthalate without any deliberately added catalyst or inhibitor. This form of curve was followed closely (±3 min., ±2 ml.) on repetition with samples from one batch of metabisulphite and phthalate, and with a somewhat greater scatter with varying sources of material.

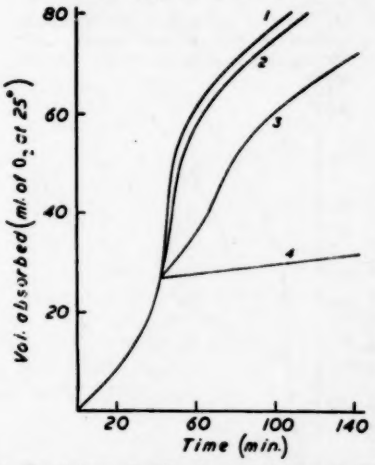
The uptake of oxygen in curve 1 amounted to only about one-third of the theoretical for $HSO_3^- \longrightarrow HSO_4^-$. Analysis, by iodine titration, showed that the sulphite removed corresponded accurately to the oxygen uptake, and it was difficult to demonstrate convincingly that any dithionate was formed. As HSO_4^- is a much stronger acid than HSO_3^-, the solution, despite the buffer action, has a tendency to become more acid and to deposit phthalic acid.

FIG. 1. *Oxygen absorption by bisulphite at* pH 4, *showing effect of injection of potassium ferricyanide solution.*



1, Untreated; 2, 10^{-7}M-; 3, 10^{-6}M-; 4, 10^{-5}M-$K_4Fe(CN)_6$; 5, 10^{-6}M-Cu^{2+}.

FIG. 2. *Oxygen absorption by bisulphite solution at* pH 4, *showing effect of withdrawal of oxygen for various periods.*



1, No delay; 2, 10 minutes' delay; 3, 78 minutes' delay; 4, 18 hours' delay.

Attention was then focused on the sensitivity of the reaction to catalysis and inhibition. Curves 2, 3, and 4 show the effect of the injection into the solution of small amounts of relatively concentrated potassium ferrocyanide solution. An amount sufficient to bring the overall concentration to 10^{-7}M has a perceptible retarding action. Fluoride and phosphate show little activity. Conversely, the initial addition of copper salts (see curve 5, Fig. 1) decreases the induction period and increases the maximum observed rate. No doubt very low concentrations of catalysts were initially present in the buffer reaction medium; analysis of the solid sulphite and phthalate by complete oxidation followed by spot tests indicated concentrations of 10^{-7}M at most. Chromic ion, a possible contaminant from the " chromic acid " cleansing of the glassware, is non-catalytic.

In an attempt to obtain more information, the reaction was stopped at a definite early stage by withdrawal of the oxygen supply and then re-started after a delay. For delays of a few minutes the aqueous medium was deprived of oxygen simply by stopping the shaking so that the oxygen uptake through the liquid surface became negligible; for longer periods the oxygen was displaced by nitrogen or carbon dioxide.

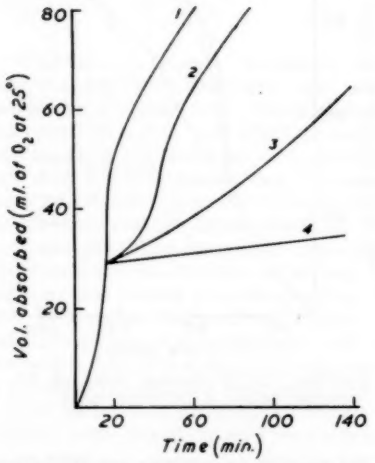
Fig. 2, curve 1, shows the course of the adsorption normally obtained without added catalyst. Curves 2, 3, and 4 show the form of the subsequent reaction when a solution initially following curve 1 is stopped after 27 ml. of adsorption and deprived of oxygen for 10 min., 78 min., and

18 hr. respectively. For convenience in display, the duration of the delay is omitted from the time curves. The curves for absorption after the delay show neither the form given initially by the system nor the form expected had there been no delay.

Two explanations seem possible. During the delay, either some inhibitor has found its way into the reaction medium or some catalyst present and functioning at the stop-point has been lost. The glass walls of the vessel, the grease on the three-way tap between flask and burette, the gas present in the flask during the delay, and the mercury in the burette appear the only possible sources of contamination. Various experiments have been carried out to eliminate these factors. Paraffin-lined vessels, silver-plated vessels, all-silica reaction vessels, phosphoric acid and Silicone greases as lubricant, delays with the flask evacuated, and water in the burette instead of mercury, were all tried but in each case a very similar delay effect was observed. Inhibition seems eliminated as the cause.

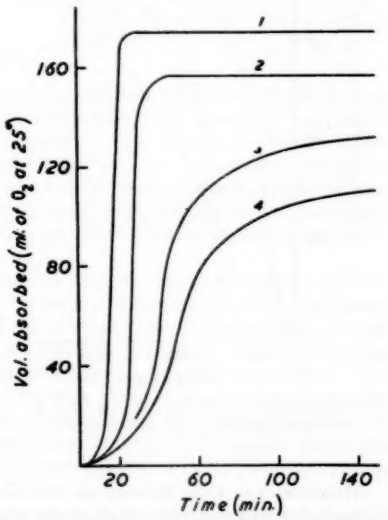
Loss of catalyst by adsorption on the surface of the Pyrex vessels was shown to be of no importance by carrying out runs with the addition of many grams of well-washed finely ground Pyrex glass. Similarly, the delay experiments gave the same results when the aqueous medium

FIG. 3. *Oxygen absorption by bisulphite solution at* pH 4 *with added* Cu^{2+} (10^{-6}M), *and showing the effect of various delays.*



1, No delay; 2, 24 hours' delay; 3, 72 hours' delay; 4, 240 hours' delay.

FIG. 4. *Oxygen absorption by bisulphite solution at* pH 4 *with* Mn^{2+} *at various concentrations as catalyst.*



1, 10^{-3}M; 2, $0{\cdot}5 \times 10^{-3}$M; 3, 10^{-3}M; 4, 10^{-4}M.

contained finely powdered silica or barium sulphate. We conclude that the variation in reaction rate is due to the loss of an initially present catalyst from the solution by some process such as slow complex-formation with the sulphite–buffer system or dispersion as a colloidal phase.

Further results are presented in Fig. 3, where the same delay technique has been applied to a reaction mixture originally made 10^{-6}M in Cu^{2+}. A 10-day delay here greatly reduces the effectiveness of the copper catalysis. Similar results were obtained at 10^{-5}M-Cu^{2+} and 10^{-4}M-Cu^{2+}.

The phenomenon is not peculiar to cupric catalysis of the reaction. Fig. 4 shows the oxidation of HSO_3^- by oxygen in presence of Mn^{2+}. The family of curves differs from the corresponding series for Cu^{2+} in that oxidation is carried much nearer completion in comparable times. This may be considered as due to the catalytic mechanism's being much less adversely affected by increasing acidity in the Mn^{2+} than in the Cu^{2+} case. Fig. 5 shows a series of delay experiments carried out with Mn^{2+} at 10^{-4}M. Further results showed that even at 10^{-3}M-Mn^{2+}

the catalytic effect could be counterbalanced by a sufficiently long delay. The extremely active catalytic nature of Mn^{2+} towards the system oxygen–saturated sulphur dioxide–water was pointed out by Bassett and Parker.[1] Hoather and Goodeve [2] performed similar experiments in which the oxygen uptake for Mn^{2+} catalysis proceeded rapidly at a constant rate until near completion, thus paralleling our results in Fig. 4.

Acetic acid–sodium acetate and citric acid–disodium hydrogen phosphate buffers showed similar general behaviour for the absorption after a delay, though the details were different.

The phenomena observed are consistent with the viewpoint that HSO_3^- in aqueous solution at pH 4 reacts slowly with Cu^{2+} and Mn^{2+} in such a way as to reduce their ability to catalyse the oxidation of the HSO_3^-. Experiments have been performed to cause reaction of Cu^{2+} and Mn^{2+} with HSO_3^- under various conditions. Several solid products have been obtained from

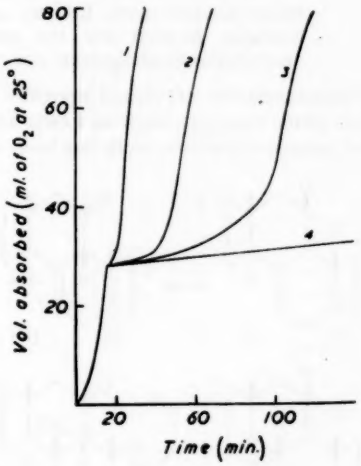


FIG. 5. *Oxygen absorption by bisulphite solution at* pH 4 *catalysed by* 10^{-4}M-Mn^{2+}, *showing effect of various delays.*

1, 1 Hour's delay; 2, 13½ hours' delay; 3, 70 hours' delay; 4, 240 hours' delay.

Cu^{2+} and will be described shortly, but no such solids have been produced from Mn^{2+}. During the delay experiments with Cu^{2+} and sulphite some separation of a copper-containing solid phase occurs; with the lowest copper concentrations this precipitation is best demonstrated by its red Tyndall beam. The slow re-dissolution of this copper material during the subsequent oxidation accounts for the observation that with Cu^{2+} catalysis the second maximum rate, especially after long delays, does not equal the expected value, whereas with Mn^{2+} the second maximum rate is much the same for all delays and similar to the expected maximum for a non-delayed run.

One of us (W. R. C.) thanks the University of Otago for a scholarship.

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[1] Bassett and Parker, *J.*, 1951, 1540.
[2] Hoather and Goodeve, *Trans. Faraday Soc.*, **1934**, **30**, 1149.

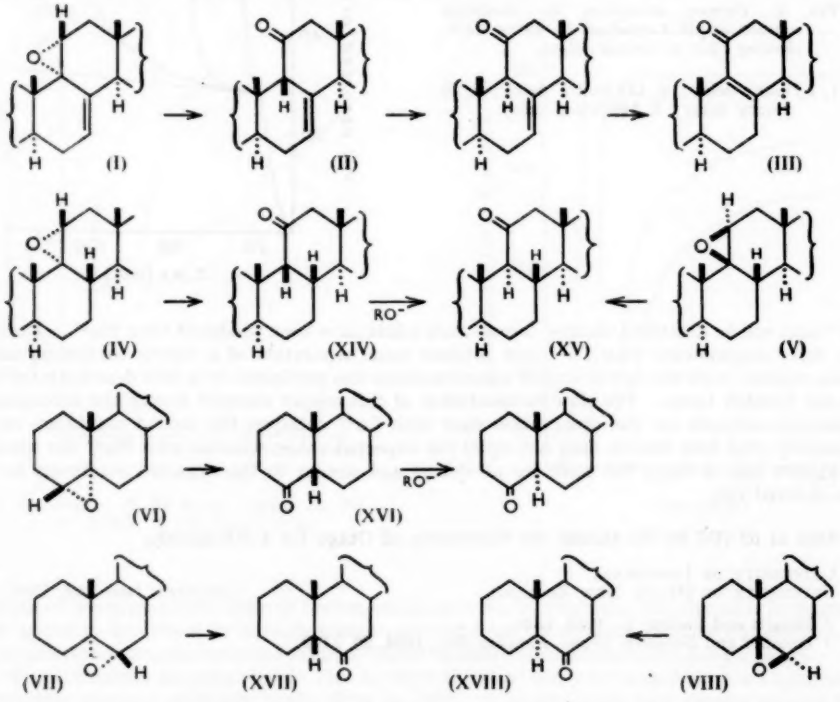
923. *Aspects of Stereochemistry. Part VI.* Reactions of Some Epoxy-steroids with the Boron Trifluoride–Ether Complex.*

By H. B. Henbest and T. I. Wrigley.

The reactions of several simple tri- and tetra-alkylated epoxides of the steroid series with the boron trifluoride–ether complex in benzene solution have been examined. Ketones or conjugated dienes appear to be formed as primary reaction products, the former arising by stereospecific hydride shifts.

Two more examples of the formation of vicinal epoxides by reduction of bromo-ketones with lithium aluminium hydride are described. These reactions proceed *via* the complex anions of diaxial bromohydrins, diequatorial bromohydrins not cyclising under the same conditions.

Rearrangements of vicinal epoxides to carbonyl compounds are catalysed by many electrophilic reagents, such as Lewis acids. In the case of purely aliphatic epoxides the most extensive previous work has been carried out by the French school [1] using magnesium



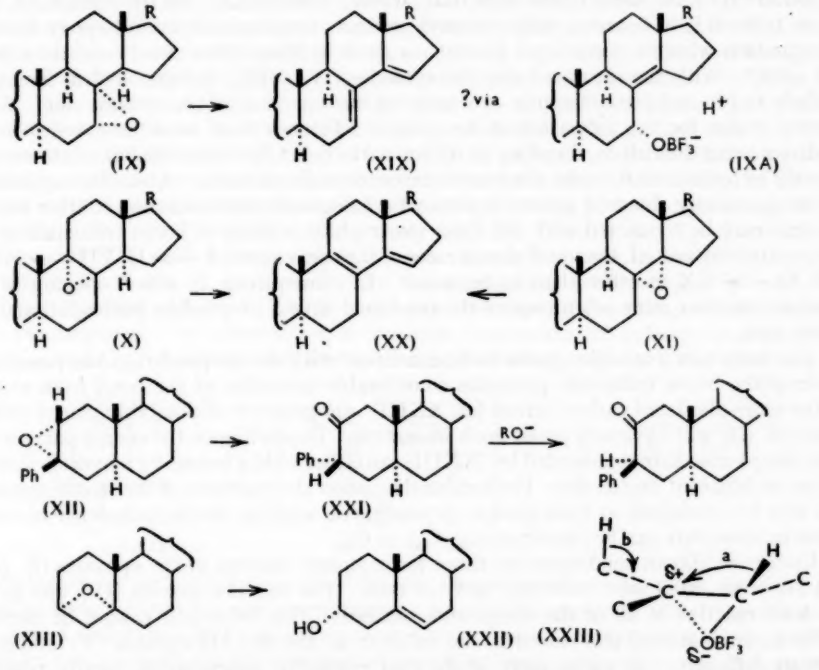
bromide in ethereal solution as catalyst. In general it was found that magnesium derivatives of bromohydrins, >CBr·C(O·MgBr)<, were formed first in such reactions, but that when heated or kept these derivatives were transformed into aldehydes or ketones with loss of magnesium bromide. In more recent years the availability and reactivity of boron trifluoride have led to the employment of this Lewis acid in a variety of reactions. In

* Part V, *J.*, 1957, 1982.

[1] Cf., *inter al.*, Tiffeneau and Tchoubar, *Compt. rend.*, 1938, **207**, 918.

particular, House and his co-workers [2] have studied its reactions with the epoxy-stilbenes and with many aryl substituted αβ-epoxy-ketones, and have shown that isomerisations of the epoxy-function to a carbonyl group may be accompanied by 1 : 2-shifts of phenyl or benzoyl groups.

In order to initiate enquiry into the reactions of purely aliphatic epoxides with boron trifluoride, compounds of the steroid series have been chosen for study. Apart from material aspects of availability of suitable epoxides and the crystallinity of starting materials and products, advantages of investigation in this series were (*a*) that stereochemical changes could be expected to be discerned easily and (*b*) that the reactions could be followed polarimetrically, thus providing information about relative velocities as well



as making it easier to stop each experiment when the initial stage of the reaction was complete. This last consideration proved of some importance as it was found that the reactive catalyst was usually able to cause further (slower) reactions, thus complicating the isolation of primary products. The only steroid reaction subjected previously to thorough scrutiny illustrates the value of polarimetric measurements, for after the first report [3] that the 9α : 11α-epoxy-Δ^7-compound (I) * could be isomerised by boron trifluoride to an 11-oxo-Δ^8-steroid (III), it was shown [4,5] that the strongly lævorotatory 9β-compound (II) was an intermediate which could be isolated in excellent yield after a brief reaction time.

The epoxides (IV—XI) have now been treated with boron trifluoride in benzene

* Partial steroid formulæ are used in this paper.

[2] House and his co-workers, *J. Amer. Chem. Soc.*, 1954, **76**, 1235; 1955, **77**, 6525; 1956, **78**, 2298, 4394.

[3] Heusser, Eichenberger, Kurath, Dallenbach, and Jeger, *Helv. Chim. Acta*, 1951, **34**, 2106.

[4] Bladon, Henbest, Jones, Lovell, Wood, and Woods; Elks, Evans, Hathway, Oughton, and Thomas, *J.*, 1953, 2921.

[5] Heusler and Wettstein, *Helv. Chim. Acta*, 1953, **36**, 398.

solution at room temperature to give the products shown (XIV—XX). Also included in the formulæ are the phenyl-substituted epoxide (XII), a preliminary report of whose isomerisation to the ketone (XXI) has been given,[6] and 3 : 5-epoxycholestane (XIII) which has been shown [7] to be readily isomerised to *epi*cholesterol.

The ketonic products of these reactions all arise by *cis*-shifts of hydrogen, thus establishing the general nature of the reaction first observed with the formation of the ketone (II) from the epoxide (I). In five cases it may be noted that this stereospecificity causes the formation of the ketonic isomer with the less stable adjacent bridgehead configuration.

Previous work,[1,2] with magnesium bromide and boron trifluoride (both in ethereal solution) has shown that bromohydrins and fluorohydrins can be initial products, but may be converted by the same Lewis acids into carbonyl compounds. On the other hand, with boron trifluoride in benzene, only carbonyl products were isolated from αβ-epoxy-ketones, the question whether these were formed *via* fluorohydrins under these conditions being left open.[2] With the saturated alicyclic epoxides (IV—VIII), halogenohydrin formation is likely to proceed predominantly or wholly by *trans*-opening of the epoxide ring. Satisfactory routes for the formation of the observed ketones from *trans*-fluorohydrin intermediates being difficult to visualise, we incline to the belief that these aliphatic ketones arise directly by hydride shifts under the present experimental conditions. A possible explanation for the previously observed greater tendency for halogenohydrin formation in ether than in benzene may be connected with the lower electrophilic activity of boron trifluoride in the oxygenated solvent (cf. the much slower rates of the conversions, I ⟶ II, VII ⟶ XVII, and XI ⟶ XX in ether than in benzene). In consequence, in ether, opening of the epoxide ring may more often require the combined attack of a halide nucleophil and the Lewis acid.

The facts now available appear to be consistent with the proposal that the powerfully electrophilic boron trifluoride promotes considerable ionisation of the bond from oxygen to the more alkylated carbon centre (cf. XXIII): the presence of a suitably placed olefinic bond [cf. (I)] will obviously assist such ionisation. Depending on the energy paths available, the intermediate represented by (XXIII) can either yield a ketone by a hydride shift (a) or lose an adjacent proton (b). For further discussion the reactions of the steroid epoxides will now be considered in three groups, depending on whether the electron-deficient centre in the intermediate can be placed on $C_{(9)}$, $C_{(5)}$, or $C_{(8)}$.

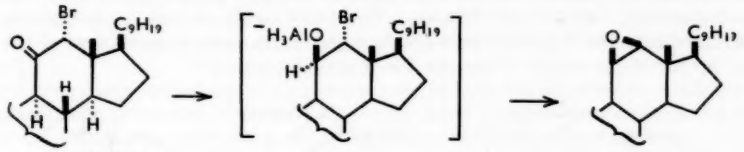
Under the chosen conditions the times for complete reaction of the epoxides (I), (IV), and (V) were <0·5 min., ~70 hr., and ~5 min. The 9α : 11α-epoxide (IV) was by far the least reactive of all of the compounds studied. This behaviour cannot be ascribed solely to an inaccessibility towards the catalyst as the 9β : 11β-epoxide (V) isomerises without difficulty. It seems more likely that relatively unfavourable energy relations are connected with the necessity of converting ring B or ring C into a boat conformation [4] in the formation of the 9β : 11-ketone (XIV): a similar conformational inhibition does not arise in the production of the 9α-11-ketone (XV). The exceedingly rapid isomerisation of the unsaturated epoxide (I), despite the concomitant creation of a 9β-configuration, is clearly caused by resonance participation of the 7 : 8-double bond.

The reactions of boron trifluoride with the epoxides (VI) and (VIII) were complete within a few minutes and the ketonic products (XVI) and (XVIII) were readily isolated. Under similar conditions the 5α : 6α-epoxide (VII) was partly unchanged and only by careful chromatography was it possible to separate the expected ketone (XVII) from non-crystalline products. In exhibiting some reluctance for the occurrence of a hydride shift to an unfavourable bridgehead configuration, this epoxide resembles the 9α : 11α-epoxide discussed above. The ease of reaction with the 4α : 5α-epoxide (which also affords a 5β-compound) may be connected with the greater flexibility of the terminal ring wherein reaction takes place.

[6] Cookson and Hudec, *Proc. Chem. Soc.*, 1957, 24.
[7] Clayton, Henbest, and Smith, *J.*, 1957, 1982.

A 1 : 3-hydride shift (or two 1 : 2-shifts) does not take place on treatment of the 3α : 5α-epoxide (XIII) with boron trifluoride. Loss of a proton from $C_{(6)}$ by the alternative reaction gives *epi*cholesterol in high yield.[7]

Although a hydride shift in the 7α : 8α-epoxide (IX) would yield a 7-ketone with a stable 8β-configuration, the 7 : 14-diene (XIX) is formed instead in a rapid reaction. The allylic alcohol derivative (cf. IXA) formed initially in this reaction contains the very stable 8(14)-double bond, and this circumstance apparently contributes driving force for the reaction observed. As the formation of the 8(14)-olefinic intermediate is in effect a *cis*-elimination it may be produced *via* a strongly developed 8-carbonium ion. The subsequent transformation of an intermediate such as (IXA) into the 7 : 14-diene (XIX) may be represented in several ways. The 7 : 14-diene actually obtained was not quite pure (from optical rotation evidence): other possible products are (*a*) the 6 : 8(14)-diene formed by loss of boron trifluoride and water towards $C_{(6)}$ from the intermediate (IXA), (*b*) the 7 : 9-diene produced *via* an 8(9)-unsaturated intermediate analogous to (XA), and (*c*) the 8(9) : 14-diene formed by partial isomerisation of the 7 : 14-diene. That the last isomerisation can occur (? catalysed by hydrogen fluoride) under the reaction conditions was shown by the isolation of the 8(9) : 14-diene (XX) when the reaction solution was kept for 24 hr. This isomerisation was first detected polarimetrically. As the 8(9) : 14-diene so formed was also not pure (not sufficiently lævorotatory) it seems probable that some non-isomerisable 7 : 9-diene is formed initially along with the 7 : 14-diene. Treatment of the 7 : 8-epoxide (IX) with mineral acid in aqueous dioxan has been shown to yield a 3 : 2 mixture of 7 : 9- and 7 : 14-dienes.[8] The two tetrasubstituted epoxides (X) and (XI) both gave the 8(9) : 14-diene (XX) in rapid reactions, and intermediates similar to (XA) may be suggested. No information is available concerning the relative importance of $C_{(8)}$, $C_{(9)}$, and $C_{(14)}$ as electron-deficient centres in the initial stages of these reactions.



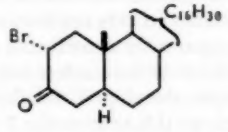
(XXIV) (XXV)

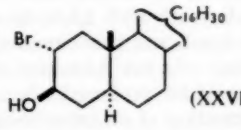
Reduction of Bromo-ketones with Lithium Aluminium Hydride.—For the foregoing investigation, compounds were required with an epoxide group in various positions in the steroid molecule. Many were known or were prepared by standard methods, but two epoxides have been obtained by reactions of suitable bromo-ketones with controlled amounts of lithium aluminium hydride. This reaction was discovered [9] in the case of a 9α-bromo-11-ketone where it may be visualised as proceeding *via* the complex anion of the diaxial bromohydrin. The 9α-bromo-11-ketone (3β-acetoxy-9α-bromoergostan-11-one) was isomerised by hydrogen bromide to a 12α-bromo-11-ketone (cf. XXIV), the reaction being accelerated by the addition of some benzoyl peroxide. Controlled reduction of this new bromo-ketone with hydride afforded an 11β : 12β-epoxide (cf. XXV). With an excess of the reducing agent the 11β-alcohol was formed. Together with infrared evidence, these reactions suffice to prove the structure of the bromo-ketone (XXIV).

This method has also been used to prepare 5β : 6β-epoxycoprostane (cf. VIII) from the new 5α-bromocholestan-6-one. This β-epoxide had been isolated previously [10] (unspecified yield and rotation) as a by-product in the reaction of cholest-5-ene with a peroxyacid. In our hands this reaction gave material inferior in quality to that obtained by the hydride reaction. Later another method was devised which gave even purer β-epoxide.[11]

[8] Alt and Barton, *J.*, 1954, 1356.
[9] Henbest, Jones, Wagland, and Wrigley, *J.*, 1955, 2477.
[10] Furter, Ruzicka, and Thomann, *Helv. Chim. Acta*, 1933, **16**, 327.
[11] Hallsworth and Henbest, following paper.

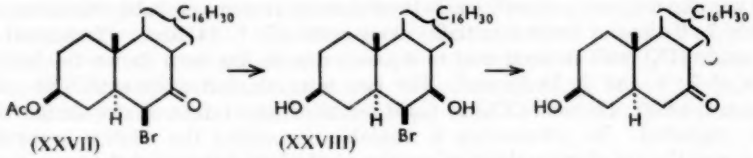
Three other bromo-ketones have been reduced with lithium aluminium hydride. 2α-Bromocholestan-3-one afforded a good yield of the diequatorial 2α-bromo-3β-alcohol (XXVI). Previous workers [12, 13] reduced this ketone with sodium borohydride, obtaining mixtures of the 3α- and the 3β-alcohol.





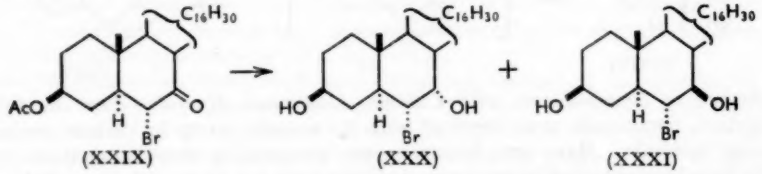
(XXVI)

Reduction of the 6β-bromo-7-ketone (XXVII) with lithium aluminium hydride gave a single bromohydrin (XXVIII), the *cis*-relation of the groups being established by conversion into the 7-ketone on treatment with potassium *tert.*-butoxide in *tert.*-butyl alcohol. Similar reduction of the unbrominated 7-ketone has been reported [13] to give about equal parts of the epimeric 7-alcohols: the axial 6β-bromine in compound (XXVII) clearly discourages the approach of hydride from the β-face and/or rearrangement of an initial hydride–ketone complex on to the β-face of the molecule.



(XXVII) (XXVIII)

Reduction of the isomeric 6α-bromo-7-ketone (XXIX) gave a mixture of two bromohydrins, separated chromatographically. The more easily eluted *cis*-compound (XXX) was converted into the 7-ketone with alkali, whereas its *trans*-isomer afforded the 6β : 7β-epoxide, prepared previously from the 7α-bromo-6β-alcohol.[15]



(XXIX) (XXX) (XXXI)

Of the five examples of the reduction of bromo-ketones with lithium aluminium hydride, epoxides are formed directly in three cases (5 : 6-, 9 : 11-, and 11 : 12-β-oxides) where *trans*-diaxial bromohydrins (as complex anions) must be formed as intermediates; in the two cases where the complex anions of *trans*-diequatorial bromohydrins are first formed, the bromohydrins themselves are finally isolated (*i.e.*, XXVI and XXXI), more drastic alkaline conditions being required to transform them subsequently into epoxides.* Simple geometrical considerations indicate that a diaxial bromohydrin should be more readily converted into an epoxide than its diequatorial isomer, as more work must be expended in the latter case in order to twist the groups into positions favourable for intramolecular nucleophilic displacement.

* The much faster ring closure of diaxial than of diequatorial halogenohydrins in alkaline solutions has been observed (cf. ref. 16).

[12] Corey, *J. Amer. Chem. Soc.*, 1953, **75**, 4832.
[13] Fieser and Huang, *ibid.*, p. 4837.
[14] Fieser, Fieser, and Chakravarti, *ibid.*, 1949, **71**, 2226.
[15] Corey, *ibid.*, 1954, **76**, 175.
[16] Barton and Cookson, *Quart. Rev.*, 1956, **10**, 67.

Reactions of the appropriate olefins with peroxyacids have been used to prepare 8 : 9- and 8 : 14-α-epoxides.

Experimental

In all experiments with the boron trifluoride–ether complex the reagent was freshly redistilled and the apparatus and the purified steroid epoxide were thoroughly dried. "AnalaR" benzene, dried over sodium, was usually employed as solvent. Reactions were terminated by addition of aqueous sodium hydrogen carbonate with shaking. The infrared absorptions of products were in each case consistent with the structures assigned. Rotations were determined for $CHCl_3$ solutions. M. p.s were determined on a Kofler block.

Coprostan-4-one (cf. XVI).—A solution of 4α : 5α-epoxycholestane (0·148 g.) in benzene (14 c.c.) was treated with the boron trifluoride–ether complex (0·12 c.c., 3 mol.). The specific rotation of the solution changed from +57° to a constant value of +38° within 2 min. at 20°. The product was isolated quickly and crystallised from acetone, to yield coprostan-4-one (74 mg.), m. p. 108—110°, $[\alpha]_D$ +44° {Dr. R. Stevenson (Glasgow) has recorded m. p. 109—110°, $[\alpha]_D$ + 41°}. A solution of this ketone (28 mg.) in benzene (1 c.c.) was adsorbed on to alumina (4 g.). After 20 hr. benzene was added to elute a solid (25 mg.), which crystallised from aqueous acetone, to give cholestan-4-one, m. p. and mixed m. p. 96—98°, infrared spectrum identical with that of an authentic sample.

Coprostan-6-one (cf. XVII).—A solution of 5α : 6α-epoxycholestane (2·31 g.) in benzene (31 c.c.) was treated with the boron trifluoride–ether complex (1·2 c.c., 1·8 mol.). Within 2 min. the specific rotation changed from −55° to a constant value of −5° (8 days were required for this change in ether solution), and the product was then isolated and chromatographed on deactivated alumina (150 g.). Elution with light petroleum gave impure starting material (0·32 g., 12%), m. p. 72—75°, $[\alpha]_D$ −47°. Elution with light petroleum–benzene (20 : 1) gave an oil (0·57 g., 33%), $[\alpha]_D$ +36°, showing hydroxyl but no carbonyl absorption in the infrared spectrum. Further elution with the same solvent mixture gave coprostan-6-one (0·555 g., 30%), m. p. 131—132° (from acetone), $[\alpha]_D$ −40° (lit.,[17] m. p. 133°, $[\alpha]_D$ −44°). Elution with benzene–ether (20 : 1) gave an oil (0·41 g., 18%), $[\alpha]_D$ +6°, showing hydroxyl but no carbonyl absorption (infrared).

A solution of coprostan-6-one (2·4 g.) in benzene (50 c.c.) was adsorbed on to alumina (100 g., impregnated with potassium hydroxide [18]). After 2 hr. addition of benzene eluted cholestan-6-one (2·4 g.), m. p. and mixed m. p. 98—100° after crystallisation from acetone.

Cholestan-6-one (cf. XVIII).—A solution of 5β : 6β-epoxycholestane (91 mg.) in benzene (10 c.c.) was treated with the boron trifluoride–ether complex (0·1 c.c., *ca.* 3 mol.). The specific rotation of the solution changed from −9° to a constant value of 0° during 4 min., and the product (90 mg.) was then isolated. One crystallisation from acetone yielded cholestan-6-one, m. p. and mixed m. p. 97—98°, infrared spectrum identical with that of an authentic sample.

3β-*Acetoxy*-9β-*ergostan*-11-*one* (cf. XIV).—A solution of 3β-acetoxy-9α : 11α-epoxyergostane (0·511 g.) in benzene (15 c.c.) was treated with the boron trifluoride–ether complex (0·4 c.c., 3 mol.) at 20°. The solution attained a constant specific rotation after 70 hr., then the product was isolated with ether and chromatographed on deactivated alumina (40 g.). Elution with light petroleum–benzene (4 : 1) afforded 3β-acetoxy-9β-ergostan-11-one (0·14 g., 25%), m. p. and mixed m. p. 155—157°, $[\alpha]_D$ +41°, infrared spectrum identical with that of an authentic sample. Elution with benzene gave an oil (0·27 g.) showing hydroxyl absorption (infrared).

3β-*Acetoxyergostan*-11-*one* (cf. XV).—A solution of 3β-acetoxy-9β : 11β-epoxyergostane [9] (0·143 g.) in benzene (14 c.c.) was treated with the boron trifluoride–ether complex (0·08 c.c., 3 mol.) at 20°. The specific rotation of the solution changed from +23° to a constant value of −2° during 5 min. The product was chromatographed on deactivated alumina (10 g.), elution with light petroleum–benzene (4 : 1) affording 3β-acetoxyergostan-11-one (51 mg.), m. p. and mixed m. p. 138—140° (from methanol), $[\alpha]_D$ +38°, infrared spectrum identical with that of authentic material. Elution with light petroleum–benzene (1 : 1) gave an oil (60 mg.), showing hydroxyl absorption (infrared).

[17] James and Shoppee, *J.*, 1955, 2885.
[18] Cf. Castells and Fletcher, *J.*, 1956, 3245.

Action of Boron Trifluoride on a 7α : 8α-*Epoxide* (IX).—A solution of 3β-acetoxy-7α : 8α-epoxyergost-22-ene [8] (0·42 g.) in benzene (15 c.c.) was treated with the boron trifluoride–ether complex (0·3 c.c., 2·9 mol.) at 20°. The specific rotation of the solution changed from −12° to −188° during 30 sec. The product was twice crystallised from methanol–acetone, giving slightly impure 3β-acetoxyergosta-7 : 14 : 22-triene (0·26 g.), m. p. 142—144°, $[\alpha]_D$ −182° (Found: C, 82·5; H, 10·7. Calc. for $C_{30}H_{46}O_2$: C, 82·15; H, 10·55%), $\lambda_{max.}$ 2420 Å (ε 11,000) in EtOH {lit., m. p. 140—141°, $[\alpha]_D$ −212°, $\lambda_{max.}$ 2420 Å (ε 9900)}.

In another experiment [starting from epoxide (0·378 g.)] the solution was kept at 20° for 24 hr., by which time the rotation had reached a constant value of −25°. The product (0·322 g.) was chromatographed on alumina (20 g.). Elution with light petroleum–benzene (4 : 1) afforded a solid which on crystallisation from methanol yielded impure 3β-acetoxyergosta-8 : 14 : 22-triene, m. p. 138—141°, $[\alpha]_D$ −28°, $\lambda_{max.}$ 2500 Å (ε 15,400) (in EtOH) {lit., m. p. 140—141°, $[\alpha]_D$ −54°, $\lambda_{max.}$ 2490 Å (ε 15,500)}.

Action of Boron Trifluoride on an 8α : 9α-*Epoxide* (X).—A solution of 3β-acetoxy-8α : 9α-epoxyergostane (46 mg.; preparation below) in benzene (7 c.c.) was treated with the boron trifluoride–ether complex (0·05 c.c., 3·9 mol.) at 20°. The rotation rapidly attained a constant negative value, and the product was isolated after 2 min. Crystallisation from methanol afforded 3β-acetoxyergosta-8 : 14-diene, m. p. and mixed m. p. 138—140°, $[\alpha]_D$ −31°, $\lambda_{max.}$ 2490 Å (ε 18,400) (in EtOH) (lit., m. p. 137—138°, $[\alpha]_D$ −28·5°).

Action of Boron Trifluoride on an 8α : 14α-*Epoxide* (XI).—Treatment of 3β-acetoxy-8α : 14α-epoxyergostane (0·564 g.; preparation below) with the boron trifluoride–ether complex (3 mol.) in benzene (25 c.c.) at 20° resulted in a change of rotation from +12° to +34° within 2 min. The product was then isolated and chromatographed on deactivated alumina (40 g.), light petroleum–benzene (1 : 1) eluting 3β-acetoxyergosta-8 : 14-diene (0·495 g.), m. p. and mixed m. p. 140—141°, $[\alpha]_D$ −38°, $\lambda_{max.}$ 2490 Å (ε 18,600) in EtOH.

A similar reaction in ether required 15 days for the rotation to reach a constant value. Isolation gave the same diene as before.

Preparation of Epoxides.—3β-*Acetoxy*-11β : 12β-*epoxyergostane* (cf. XXV). A solution of 3β-acetoxy-12α-bromoergostan-11-one (0·39 g.) and lithium aluminium hydride (23 mg., 0·83 mol.) in ether (25 c.c.) was heated under reflux for 45 min. The product was isolated with ether, acetylated, and chromatographed on deactivated alumina (30 g.). Elution with light petroleum–benzene (5 : 1) gave the 11β : 12β-*epoxide* (123 mg.), m. p. 133—135° (from methanol), $[\alpha]_D$ +29° (Found: C, 78·2; H, 11·1. $C_{30}H_{50}O_3$ requires C, 78·55; H, 11·0%). No other crystalline products were obtained by further elution of the chromatogram.

When a solution of the 12α-bromo-11-ketone (0·15 g.) and lithium aluminium hydride (0·2 g.) in tetrahydrofuran (20 c.c.) was heated under reflux for 4 hr., and the product isolated with ether and crystallised from methanol, ergostane-3β : 11β-diol, m. p. and mixed m. p. 177—179°, was obtained. Acetylation gave 3β-acetoxyergostan-11β-ol, m. p. and mixed m. p. 132—133°.

5β : 6β-*Epoxycholestane* (cf. VIII). A solution of cholestan-6-one (0·939 g.) in ether (25 c.c.) and acetic acid (7 c.c.) was treated with a solution of bromine in acetic acid (4·69 c.c. of a 2·8% v/v solution, 1·05 mol.). The bromine colour was discharged during 30 sec. at 20°. Water was then added and the steroid isolated with ether. Crystallisation from acetone gave 5α-*bromocholestan-6-one* (0·827 g., 70%), m. p. 101—102°, $[\alpha]_D$ −134° (Found: C, 70·15; H, 9·85; Br, 17·75. $C_{27}H_{45}OBr$ requires C, 69·65; H, 9·65; Br, 17·25%).

The molecular-rotation difference between this bromo-ketone and cholestan-6-one is −635°, in excellent agreement with that (−630°) between 3β-acetoxy-5α-bromocholestan-6-one and its 5-hydrogen analogue, but different from that (+282°) between 3β-acetoxy-7α-bromocholestan-6-one and the unbrominated compound.

A solution of the bromo-ketone (0·638 g.) and lithium aluminium hydride (14 mg., 0·27 mol.) in ether (20 c.c.) was heated under reflux for 10 min. The product was isolated with ether and chromatographed on alumina (25 g.). Elution with light petroleum gave 5β : 6β-epoxycholestane (0·142 g.), m. p. 55—57° (from acetone), $[\alpha]_D$ −9° (Found: C, 83·7; H, 12·0. Calc. for $C_{27}H_{46}O$: C, 83·85; H, 12·0%). Further elution with the same solvent afforded impure starting material (87 mg.), m. p. 81—93° (from acetone). Elution with benzene gave a gum (0·245 g.).

5α : 6α-*Epoxycholestane* (cf. VII). Perbenzoic acid in benzene (475 c.c. of a 0·21M-solution; 1·3 mol.) was added to a solution of cholest-5-ene (29 g.) in benzene (50 c.c.), and the mixture was kept at 20° for 2 hr. Organic acids were washed out with aqueous potassium hydrogen

carbonate, and the benzene solution was filtered through deactivated alumina (650 g.), the adsorbent being washed with more benzene. Removal of solvent gave material (29 g.) which after 5 crystallisations from acetone gave the pure α-epoxide (8·4 g.), m. p. 74—75°, $[\alpha]_D$ −55°. A portion of this product was separated into 16 fractions by chromatography on deactivated alumina; the rotation of each fraction was $[\alpha]_D$ −56° ± 3°, and crystallisation of some of the fractions only altered the m. p. slightly, to 75—76°.

Reduction of the α-epoxide (0·729 g.) with an excess of lithium aluminium hydride in boiling ether gave cholestan-5α-ol (0·591 g., 81%), m. p. 100—102°. No cholestan-6β-ol was obtained.

Material (8 g.) from the first mother-liquor from crystallisation of the α-epoxide was chromatographed on deactivated alumina (800 g.). Light petroleum (b. p. 40—60°) was used as eluting solvent and most of the material was eluted in thirty 100 c.c. fractions. The rotations of all of these were within −16° to −19°. Crystallisation of the products from various fractions gave impure β-epoxide: a typical sample had m. p. 60—63°, $[\alpha]_D$ −18°.

2α-Bromocholestan-3β-ol (cf. XXVI).—A solution of 2α-bromocholestan-3-one (0·528 g.) and lithium aluminium hydride (0·3 g.) in ether (30 c.c.) was heated under reflux for 2 hr. The product (0·41 g.) was isolated with ether, and a portion (0·246 g.) was chromatographed on deactivated alumina (20 g.). Elution with light petroleum–benzene (1 : 1) afforded pure 2α-bromocholestan-3β-ol (0·215 g.), double m. p. 76° and 112—114° (from methanol), $[\alpha]_D$ +19°. Acetylation yielded 3β-acetoxy-2α-bromocholestane, m. p. 106—107° (from methanol), $[\alpha]_D$ −4°. Recorded values [12, 13] are: for the bromohydrin, m. p. 111·5—112·5° $[\alpha]_D$ +14° and m. p. 113—114°, $[\alpha]_D$ +12°, and for the acetate, m. p. 106—107°, $[\alpha]_D$ −82°. Professor L. F. Fieser, Harvard, has informed us that this rotation should be −8·2°.

Reduction of 3β-Acetoxy-6β-bromocholestan-7-one (XXVII).—A solution of the steroid (0·935 g.) and lithium aluminium hydride (0·2 g.) in ether (150 c.c. was heated under reflux for 1 hr. Isolation with ether followed by crystallisation from acetone yielded the *bromohydrin* (XXVIII) (0·56 g.), m. p. (decomp.) 183—186°, $[\alpha]_D$ +44° (Found: C, 67·15; H, 9·5; Br, 16·55. $C_{27}H_{47}O_2Br$ requires C, 67·1; H, 9·75;. Br, 16·55%).

A solution of the bromohydrin (1·8 g.) in anhydrous *tert.*-butyl alcohol (50 c.c.) was treated with molar potassium *tert.*-butoxide in the alcohol (15 c.c.) at 20°. Potassium bromide separated almost immediately and after 5 min. the product was isolated with ether and crystallised from methanol, to give 3β-hydroxycholestan-7-one (1·1 g.), m. p. 166—168°, $[\alpha]_D$ −31°.

Acetylation and crystallisation of the product from methanol afforded 3β-acetoxycholestan-7-one, m. p. and mixed m. p. 149—150°, $[\alpha]_D$ −34°.

Reduction of 3β-Acetoxy-6α-bromocholestan-7-one (XXIX).—A solution of the steroid (2·638 g.) and lithium aluminium hydride (0·158 g., 0·83 mol.) was heated under reflux for 1 hr. The product was isolated with ether and chromatographed on deactivated alumina (140 g.). Elution with benzene–ether (9 : 1) gave *6α-bromocholestane-3β : 7α-diol* (0·83 g.), m. p. 131—132° (from acetone), $[\alpha]_D$ +59° (Found: C, 67·4; H, 9·8. $C_{27}H_{47}O_2Br$ requires C, 67·1; H, 9·75%). Further elution with this solvent mixture afforded *6α-bromocholestane-3β : 7β-diol* (0·65 g.), m. p. 209—212° (from acetone), $[\alpha]_D$ +64° (Found: C, 67·3; H, 9·8; Br, 16·85%).

A solution of the 6α-bromo-3β : 7β-diol (0·75 g.) in benzene (10 c.c.) and anhydrous *tert.*-butyl alcohol (50 c.c.) was treated at 20° with M-potassium *tert.*-butoxide solution in the alcohol (12 c.c.). Potassium bromide was precipitated almost immediately and after 10 min. the product (0·622 g.) was isolated with ether. Chromatography on deactivated alumina yielded 6β : 7β-epoxycholestan-3β-ol [0·515 g., eluted with benzene–ether (9 : 1)], m. p. 154—156° (from acetone), $[\alpha]_D$ −10° (lit.,[15] m. p. 157—158°, $[\alpha]_D$ −14·5°) (Found: C, 80·5; H, 11·6. Calc. for $C_{27}H_{44}O_2$: C, 80·55; H, 11·5%). Acetylation gave *3β-acetoxy-6β : 7β-epoxycholestane*, m. p. 137—139° (crystallised from methanol), $[\alpha]_D$ −23° (Found: C, 78·4; H, 11·05. $C_{29}H_{46}O_3$ requires C, 78·2; H, 10·9%).

A solution of the 6α-bromo-3β : 7β-diol (0·246 g.) in *tert.*-butyl alcohol (15 c.c.) was treated with M-potassium *tert.*-butoxide solution in the alcohol (10 c.c.). The mixture was kept at 20° for 5 hr., then the steroid was isolated with ether. The product still gave a positive Beilstein test and was purified by chromatography on deactivated alumina (10 g.). Elution with benzene afforded 3β-hydroxycholestan-7-one (0·104 g.), m. p. and mixed m. p. 165—167°.

3β-Acetoxy-8α : 9α-epoxyergostane (cf. X).—A solution of 3β-acetoxyergost-8-ene [21] (0·3 g.)

[19] Fieser, Rosen, and Fieser, *J. Amer. Chem. Soc.*, 1952, **74**, 5397.
[20] Barton and Cox, *J.*, 1948, 783; 1949, 5397.
[21] Hallsworth, Henbest, and Wrigley, *J.*, 1957, 1969.

XUM

in benzene (11 c.c.) was treated with perbenzoic acid (5·45 c.c. of a 2·5M-solution in benzene; 2 mol.). One equivalent of peroxy-acid was consumed during 72 hr. at 0°, and the steroid was then isolated and filtered in light petroleum–benzene (2 : 1) solution through deactivated alumina (15 g.). The *epoxide* (0·264 g., 85%) had m. p. 180—183° (from methanol), $[\alpha]_D$ +4° (Found: C, 78·75; H, 11·45. $C_{30}H_{50}O_3$ requires C, 78·55; H, 11·0%).

3β-*Acetoxy*-8α : 14α-*epoxyergostane* (cf. XI).—Anhydrous formic acid (25 c.c.) and hydrogen peroxide (25 c.c. of a 30% solution in water) were added to a solution of 3β-acetoxyergost-8(14)-ene (5 g.) in chloroform (100 c.c.), and the two-phase system was then stirred for 13 hr. at 20°. After organic acids had been washed out, the chloroform was evaporated to give a yellow gum (5·1 g.) which was chromatographed on deactivated alumina (300 g.). Elution with light petroleum–benzene (9 : 1) gave the 8 : 14-*epoxide* (2·6 g., 50%), m. p. 139—140° (from methanol), $[\alpha]_D$ +15° (Found: C, 78·35; H, 10·95. $C_{30}H_{50}O_3$ requires C, 78·55; H, 11·0%).

3β-*Acetoxy*-12α-*bromoergostan*-11-*one* (cf. XXIV).—3β-Acetoxy-9α-bromoergostan-11-one (0·5 g.) and benzoyl peroxide (0·113 g., 0·5 mol.) were dissolved in acetic acid (15 c.c.) and benzene (15 c.c.), and hydrogen bromide (1 c.c. of a 50% w/v solution in acetic acid, *ca.* 12·5 mol.) was added. These operations were performed with nitrogen bubbling through the solution which was shielded from light. The specific rotation of the solution changed from +128° to a constant value of −3° after 41 hr. at room temperature. Isolation with ether and crystallisation from methanol afforded pure 3β-*acetoxy*-12α-*bromoergostan*-11-*one* (0·376 g.), m. p. 135—137°, $[\alpha]_D$ −3° (Found: C, 66·9; H, 9·5; Br, 15·0. $C_{30}H_{49}O_3Br$ requires C, 67·0; H, 9·25; Br, 14·9%). Infrared absorption (in CS_2): carbonyl peak at 1705 cm.$^{-1}$ (as in the unbrominated compound).

One of the authors (T. I. W.) thanks the Department of Scientific and Industrial Research for a Maintenance Grant. In this and the following two papers the microanalyses are by Mr. E. S. Morton and the infrared spectra were determined under the direction of Dr. G. D. Meakins.

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924. *Aspects of Stereochemistry. Part VII.* Metal Reduction of Vicinal Epoxy*cyclo*hexanes.*

By A. S. HALLSWORTH and H. B. HENBEST.

Reduction of vicinal epoxy*cyclo*hexanes of the steroid series with lithium–ethylamine is shown to yield axial alcohols. This method can be more powerful and specific than that with lithium aluminium hydride. Thus 7α : 8α- and 9α : 11α-epoxides, which are not reduced by the hydride, are converted into 8α- and 9α-alcohols by metal–amine reduction, and 5β : 6β-epoxycholestane, which yields an exceptionally high proportion (~60%) of the equatorial 5β-alcohol on reduction with hydride, gives a high yield of the axial 6β-alcohol with lithium–ethylamine. The metal–amine reactions are visualized as proceeding by attack of solvated electrons, effectively a nucleophilic reagent of low steric requirements.

APART from the isolation of propan-2-ol on treatment of propylene oxide with sodium in ammonia,[1] very little appears to be known about directing influences in the metal reduction of unsymmetrical vicinal epoxides. In order to gain some knowledge of the stereochemical course of such reactions, various epoxides of the steroid series have been reduced by the convenient lithioethylamine technique.[2]

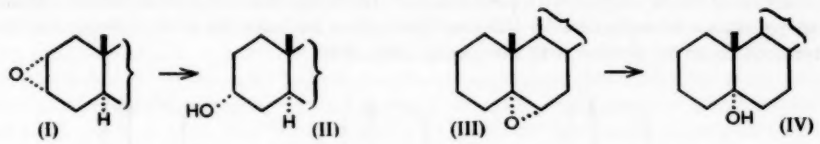
In this way, 2α : 3α- (I) † and 5α : 6α-epoxycholestane (III) gave good yields of the

* Part VI, preceding paper. † Partial steroid formulæ are used in this paper.

[1] Birch, *J. Proc. Roy. Soc. New South Wales*, 1950, **83**, 245.

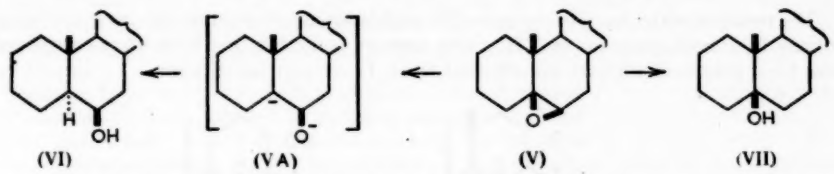
[2] (*a*) Benkeser, Robinson, Sauve, and Thomas, *J. Amer. Chem. Soc.*, 1955, **77**, 3230; (*b*) Hallsworth, Henbest, and Wrigley, *J.*, 1957, 1969.

axial alcohols (II) and (IV), the reactions proceeding in the same direction as reduction with lithium aluminium hydride,[3] Attack by the nucleophilic aluminium hydride anion is usually considered to be the chief driving force in the opening of epoxide rings by the



latter reagent: in the metal–amine reductions solvated electrons may be regarded as the corresponding nucleophil (cf. below).

Reduction of 5β : 6β-epoxycholestane [4] (V) with lithium–ethylamine gave the axial 6β-alcohol (VI) as the main product (~80%). If this reaction is depicted as proceeding



through an intermediate $C_{(5)}$-carbanion (cf VA), addition of a proton at position 5 takes place from an α-direction to give the more stable *trans*-ring fusion (as do other such reactions [5]). This reduction also afforded a small amount (6%) of the 5β-alcohol (VII), in which the hydroxyl group is equatorial to ring B wherein reaction is taking place. This was the only example where some equatorial-alcohol product was detected, perhaps because the epoxide (V) was the only trisubstituted epoxide investigated where the formation of an axial alcohol requires the nucleophil to attack at the more alkylated position.* Thus it was not surprising to find that reduction of this epoxide with lithium aluminium hydride gave less of the axial alcohol (VI), approach of the bulky aluminium hydride anion to position 5 being inhibited. The large proportion (~60%) of equatorial product (VII) obtained from this reaction with hydride is noteworthy, and appears to be the most extreme example of the violation of the rule of axial opening of epoxide rings flanked by saturated groupings.†

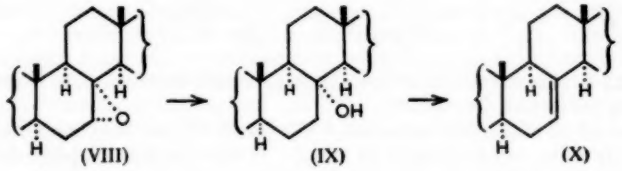
The relative bulkiness of the aluminium hydride anion also appears to be responsible for the fact that 7α : 8α- and 9α : 11α-epoxy-steroids have not been reduced to alcohols by the hydride reagent, top(β)-face approach to the centre of the steroid molecule being prevented by the angular methyl groups. Both epoxides were, however, reduced by the lithium–ethylamine method. The 7α : 8α-epoxide (VIII) gave an alcohol resistant to acetylation under the normal conditions, which is therefore the 8α-alcohol (IX): this again is an axial product, as ring B is in a boat conformation.[8] Dehydration of the 8α-alcohol with

* Attack at position 5 takes place when cholesterol β-epoxide and esters are opened with halogen acids, 5α-halogeno-6β-alcohols being formed.[6] In these reactions protonation of the epoxide-oxygen atom promotes ionization of the bond to the more alkylated 5-position, and attack of an anion at this centre is therefore encouraged. In contrast, in the present reductions, the nucleophilic is likely to be much greater than the electrophilic driving force, and the reactions are therefore more sensitive to steric factors.

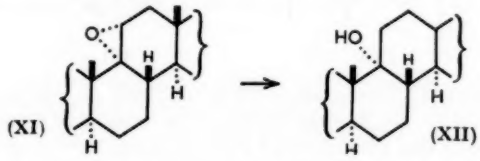
† Reduction of the related cholesterol β-epoxide with lithium aluminium hydride has been reported [7] to give a rather different ratio of products, 3β : 5β-diol (20%) and 3β : 6β-diol (60%).

[3] Fürst and Plattner, *Helv. Chim. Acta*, 1949, **32**, 275.
[4] Preparation as for cholesterol β-epoxide: Davis and Petrow, *J.*, 1949, 2536.
[5] Barton and Robinson, *J.*, 1954, 3045.
[6] Cf. Barton, Miller, and Young, *J.*, 1951, 2598.
[7] Plattner, Heusser, and Feurer, *Helv. Chim. Acta*, 1949, **32**, 587.
[8] Clayton, Henbest, and Jones, *J.*, 1953, 2015.

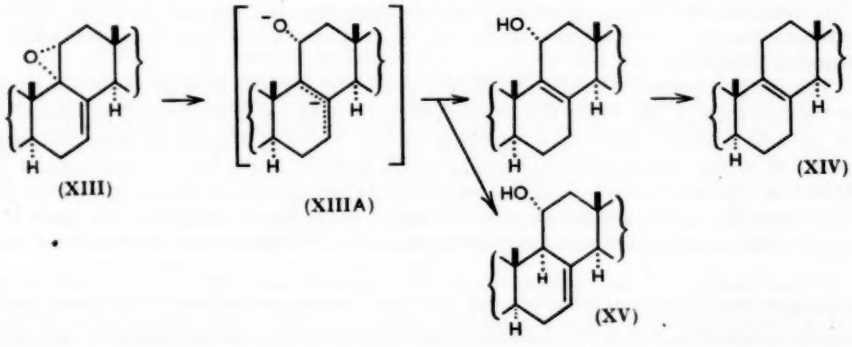
thionyl chloride in pyridine * gave the 7 : 8-unsaturated compound (X), *trans*-elimination towards position 9 or 14 being impossible. It may be noted that an α-configuration was assigned [10] to the starting epoxide (VIII) on the basis of its method of preparation from the reaction of the Δ^7-steroid with peroxyacid. In our opinion this formulation is supported by its resistance to reduction by lithium aluminium hydride, for a 7β : 8β-epoxide should be reduced to an 8β-alcohol with no special difficulty.



The reaction of the 9α : 11α-epoxide (XI) with lithium–ethylamine also generated an axial tertiary hydroxyl group (as in XII); this appears to be the first 9-hydroxy-compound to have been prepared without an adjacent 8- or 11-oxygen substituent.



Lithium reduction of the Δ^7-9α : 11α-epoxide (XIII) gave the Δ^8-compound (XIV) and the Δ^7-11α-alcohol (XV) in approximately equal amounts. The epoxide (XIII) contains an allylic ether grouping and, since reduction of allylic ethers by metals is greatly assisted by initial production of a resonance-stabilized carbanion,[2b] the reaction products probably arise from a 7 : 8 : 9-anionic intermediate (cf. XIIIA). A proton can then be provided by the solvent at (i) position 7, to give an 11α-hydroxy-Δ^8-compound which, being an allylic



alcohol, is then reduced further to the Δ^8-steroid (XIV) (the related 11β-hydroxy-Δ^8-compound undergoes this reduction [2b]) or (ii) at position 9 (at the less hindered α-face) to give the other reaction product (XV). The ready acetylation of the hydroxyl group in the

* The greater resistance of this alcohol to dehydration by dilute mineral acid compared with 5α : 8α-diols has already been discussed.[9]

[9] Henbest and Lovell, *J.*, 1957, 1965.
[10] Alt and Barton, *J.*, 1954, 1356.

latter product and its difference from the 9β-compound [11] confirm the structure assigned to it. The alternative possibility that the Δ^8-compound (XIV) is formed by initial attack of solvated electrons on the epoxide at position 11, to give a Δ^7-9α-alcohol which is further reduced, cannot, however, be wholly excluded at present.

These results seem consistent with the idea that reduction of vicinal epoxides by metals takes place by attack of solvated electrons acting as a penetrating nucleophilic reagent. Thus reduction of the hindered 7α : 8α- and 9α : 11α-epoxides shows that the steric requirements of the attacking agent cannot be high, but the isolation of a small amount of equatorial product from the 5β : 6β-epoxide (V) and the formation of propan-2-ol from propylene oxide indicate that the attacking agent has some bulk and this is in agreement with attack by solvated electrons.

Experimental

Cholestan-3α-ol (cf. II).—Reduction of 2α : 3α-epoxycholestane (0·15 g.) with lithium (75 mg.) in ethylamine (10 c.c.) [2b] gave a product which was then chromatographed on deactivated alumina (10 g.). Elution with light petroleum–benzene (1 : 1) gave material (0·105 g.) from which cholestan-3α-ol, m. p. and mixed m. p. 182°, $[\alpha]_D$ +27°, was obtained on one crystallisation from ethanol.

Cholestan-5α-ol (cf. IV).–Reduction of 5α : 6α-epoxycholestane (0·2 g.) with lithium (0·1 g.) in ethylamine (10 c.c.), followed by isolation with ether and one crystallisation from aqueous acetone, gave a high yield of cholestan-5α-ol, m. p. and mixed m. p. 109—110°, $[\alpha]_D$ +22°.

5β : 6β-*Epoxycoprostane* (cf. V).—A mixture of dry chloroform (75 c.c.), pure dimethylaniline (40 c.c.), acetyl chloride (32 c.c.), and cholestane-5α : 6β-diol (4 g.) was heated under reflux for 16 hr. The product was isolated in chloroform and chromatographed on deactivated alumina (300 g.). Elution with light petroleum gave some diene (0·13 g.), m. p. 82—83°, $[\alpha]_D$ −63° (probably therefore a mixture of the 3 : 5- and the 4 : 6-isomer), giving a deep orange colour with tetranitromethane. Elution with light petroleum–benzene (1 : 1) gave the 5α : 6β-diacetate as a gum. This was heated in absolute ethanol (200 c.c.) containing potassium hydroxide (5 g.) for 2·5 hr. Most of the alcohol was distilled off and the steroid isolated with ether. The product in light petroleum was filtered through deactivated alumina, to give the β-epoxide (3 g.), m. p. 80—81°, $[\alpha]_D$ +8°.

Reduction of 5β : 6β-*Epoxycoprostane.*—(a) *With lithium–ethylamine.* The epoxide (0·5 g.) was reduced with lithium (0·25 g.) in ethylamine (25 g.), and the product heated with acetic anhydride and pyridine at 100° for 2 hr. Chromatography on deactivated alumina (50 g.) gave 6β-acetoxycholestane (0·4 g.) (eluted by light petroleum), m. p. 77° (from methanol), $[\alpha]_D$ −7° (lit.,[12] m. p. 75°, $[\alpha]_D$ −7·5°); alkaline hydrolysis gave cholestan-6β-ol, m. p. 80—81°, $[\alpha]_D$ +8°. Further elution with light petroleum–benzene (1 : 1) yielded coprostan-5β-ol (30 mg.), m. p. 81—82° (from methanol), whose infrared spectrum was identical with that prepared by the following method.

(b) *With lithium aluminium hydride.* A mixture of the epoxide (0·5 g.) and hydride (0·5 g.) and dry ether (20 c.c.) was heated under reflux for 18 hr. The product was isolated with ether, acetylated as before, and then chromatographed on deactivated alumina (50 g.). Elution as described above gave 6β-acetoxycholestane (0·155 g.), m. p. 77°, $[\alpha]_D$ −6·5°, and *coprostan-5β-ol* (0·305 g.), m. p. 81—82°, $[\alpha]_D$ +37° (Found: C, 83·9; H, 12·5. $C_{27}H_{48}O$ requires C, 83·45; H, 12·45%). Infrared spectrum (in CS_2): OH peak at 3615 cm.$^{-1}$. This alcohol apparently separates as a solvate from methanol, the crystalline material changing to a powder on warming and/or drying.

3β-*Acetoxyergost-22-en-8α-ol* (cf. IX).—3β-Acetoxy-7α : 8α-epoxyergost-22-ene (0·5 g.) was reduced with lithium (0·2 g.) in ethylamine (25 g.). The product was isolated with ether, acetylated, and chromatographed on deactivated alumina (25 g.). Elution with benzene–light petroleum (1 : 4) afforded 3β-acetoxyergosta-7 : 22-diene (0·24 g.), m. p. and mixed m. p. 179—181°. Elution with benzene–ether (19 : 1) gave the 8α-*alcohol* (0·18 g.), m. p. 127—129° (from methanol), $[\alpha]_D$ −25° (Found: C, 78·4; H, 10·85. $C_{30}H_{50}O_3$ requires C, 78·55; H, 11·0%). Infrared spectrum (in CS_2): peaks at 3685 (OH), 1735, 1245 (OAc) and 975 cm.$^{-1}$ (Δ^{22}).

This compound (50 mg.) in pyridine (2 c.c.) was treated with thionyl chloride (0·1 c.c.) at 20°.

[11] Crawshaw, Henbest, Jones, and Wagland, *J.*, 1955, 3420.
[12] Shoppee and Summers, *J.*, 1952, 3361.

After 30 min. the product was isolated with ether, then dissolved in light petroleum and filtered through deactivated alumina. Crystallisation of this material (40 mg.) from methanol gave 3β-acetoxyergosta-7 : 22-diene, m. p. and mixed m. p. 178—181°, $[\alpha]_D$ −20°.

3β-*Acetoxyergostan*-9α-*ol* (cf. XII).—3β-Acetoxy-9α : 11α-epoxyergostane (50 mg.) was reduced with lithium (50 mg.) in ethylamine (10 c.c.), the mixture being shaken until the blue colour disappeared. The product was isolated with ether, acetylated, and chromatographed on deactivated alumina (5 g.). Elution with benzene–light petroleum (1 : 1) gave material (47 mg.) which, after one crystallisation from methanol, yielded the 9α-*alcohol*, m. p. 168—169°, $[\alpha]_D$ −1° (Found: C, 78·15; H, 11·6. $C_{30}H_{52}O_2$ requires C, 78·15; H, 11·4%). Infrared spectrum (in CS_2): peaks at 3685 (OH), 1730 and 1245 cm.$^{-1}$ (OAc).

Reduction of 3β-*Acetoxy*-9α : 11α-*Epoxyergosta*-7 : 22-*diene* (cf. XIII).—The epoxide (1 g.) was reduced with lithium (1 g.) in ethylamine (100 g.) for 2 hr. Isolation with ether and acetylation gave material (0·983 g.) which in light petroleum was adsorbed on to deactivated alumina (50 g.). Elution with light petroleum gave 3β-acetoxyergosta-8 : 22-diene (0·35 g.), m. p. and mixed m. p. 162—164°, $[\alpha]_D$ +14°. Elution with light petroleum–benzene (1 : 1) gave 3β : 11α-*diacetoxyergosta*-7 : 22-*diene* (0·31 g.), m. p. 123° (from methanol), $[\alpha]_D$ −21° (Found: C, 77·1; H, 10·1. $C_{32}H_{50}O_4$ requires C, 77·05; H, 10·1%).

We thank Glaxo Laboratories Ltd. for financial assistance to (A. S. H.) and gifts of chemicals.

King's College, Strand, London, W.C.2. [*Received, June 12th,* 1957.]

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925. *Aspects of Stereochemistry. Part VIII.* The Reaction of* cyclo-*Hex-3-enol with Perbenzoic Acid. An Improved Method for the Isolation of Water-soluble Epoxides.*

By H. B. Henbest and B. Nicholls.

In the reaction of *cyclo*hex-3-enol with perbenzoic acid the hydroxyl group exerts no detectable directing effect, approximately equal parts of the two epoxides being formed. Much improved yields of epoxy-alcohols may be obtained from the action of peroxyacids on unsaturated alcohols if organic acids are removed from the final reaction solution with calcium hydroxide. The reduction of cyclic *trans*-hydroxy-epoxides by lithium aluminium hydride can apparently take place by an intramolecular mechanism.

In Part I of this series,[1] it was shown by structural determinations and by kinetic measurements that the allylic hydroxyl group in *cyclo*hex-2-enol (I) directs *cis*-approach of peracids to the olefinic bond. The stereospecificity of this reaction has been confirmed by the isolation of the *cis*-hydroxy-epoxide (II) in an improved yield (90%) by a modified technique (see below).

(I) (II)

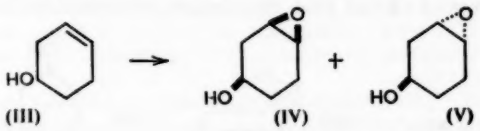
The rate of epoxidation of the corresponding βγ-unsaturated alcohol (III) is appreciably slower than that of the allylic alcohol (I) despite the fact that in the former compound the electron-attracting hydroxyl group is farther from the olefinic bond. Thus it seemed unlikely that the hydroxyl group in (III) could be exerting any considerable assisting or directing effect in the reaction with peracid: this supposition has now been confirmed by the isolation of a mixture of epoxides.

The reaction of the olefin (III) with perbenzoic acid has been reported previously,[2] a

* Part VII, preceding paper.

[1] Henbest and Wilson, *J.*, 1957, 1958.
[2] Zelinski and Titova, *Ber.*, 1931, **64**, 1399.

triol of m. p. 122° being isolated by an unspecified method. Repetition, with ether as solvent followed by the usual procedure of removing benzoic acid with aqueous potassium hydrogen carbonate, afforded hydroxy-epoxide (11%). The remainder of the material was recovered from the aqueous phase as a triol * (77%), m. p. 122—125°, apparently the

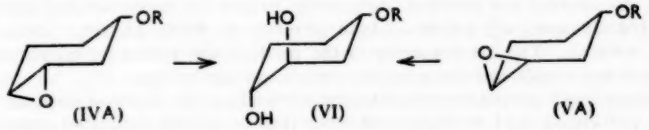


same as that described earlier. The isolation of the triol, and not its monobenzoate, indicated that hydrolysis was occurring during isolation, assisted probably by the solubility of the hydroxy-epoxide in the aqueous phase used to wash out organic acids. In agreement, neutralisation of the reaction solution by shaking with solid calcium hydroxide gave the epoxide in much higher yield. Three water-soluble epoxy-alcohols † have been prepared in good yields with the help of this method (see Table). Also the epoxide from the acetate of (III), which is only slightly soluble in water, has been obtained in yields of 89% (old method) and 95% (new method).

	Epoxide yields (%)	
	Old method	New method
*cyclo*Hex-2-enol (I)	12	90
*cyclo*Hex-3-enol (III)	11	88
But-3-enol	—	76

The epoxide mixture produced from the olefinic alcohol (III) was separated by chromatography of the α-naphthylurethanes, the crystalline *cis*- and *trans*-derivatives being obtained in 52 and 40% yield respectively. The relative configurations of these urethanes was established by reduction of the lower-melting isomer to *cyclo*hexane-*trans*-1 : 4-diol by means of lithium aluminium hydride (conformational aspects of this reaction are discussed below).

By prolongation of the contact time with chromatographic alumina, each epoxynaphthylurethane was hydrated to a higher-melting dihydroxy-compound. The formation of this product (VI; R = $CO{\cdot}NH{\cdot}C_{10}H_7$) is envisaged as proceeding by diaxial opening of either epoxide ring in the conformations shown (IVA), (VA) with the large



urethane groupings placed equatorially. The production of a single triol from the overall hydroxylation of the unsaturated alcohol (III) may be explained similarly, and this compound is therefore formulated as (VI; R = H). The formation of this triol by hydroxylation of the benzyl ether of the alcohol (III) with performic acid, followed by removal of the benzyl group (lithium in ethylamine technique [5]) strengthens the argument that, in all of these reactions, opening of the epoxide ring takes place from the conformation with the original hydroxyl group or its derived ether or urethane in an equatorial position.

* The triol (87%) was also obtained by oxidation of the olefin (III) with performic acid followed by hydrolysis of the monoformate with steam.[3]

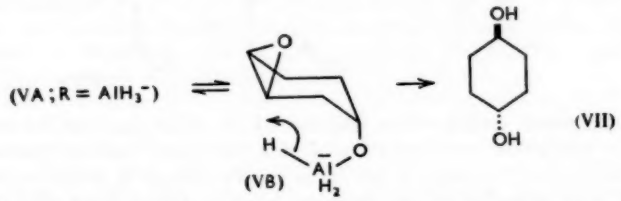
† Some aspects of the infra-red absorption of these vicinal epoxides, and of the *cyclo*hexenols (I) and (III), have been discussed recently.[4]

[3] Cf. Brown, Henbest, and Jones, *J.*, 1950, 3634.

[4] Henbest, Meakins, Nicholls, and Taylor, *J.*, 1957, 1459; Henbest, Meakins, Nicholls, and Wilson, *J.*, 1957, 997.

[5] Benkeser, Robinson, Sauve, and Thomas, *J. Amer. Chem. Soc.*, 1955, **77**, 3230.

Reduction of the epoxide mixture (IV) and (V) with lithium aluminium hydride gave *cyclo*hexane-*cis*- and -*trans*-1 : 4-diol, separated and identified as dibenzoates. The formation of the *cis*-1 : 4-diol is explicable as before, the bulky aluminium hydride complex being equatorial in the intermediate complex (IVA; R = AlH_3^-). Instead of giving *cyclo*hexane-*trans*-1 : 3-diol from the similar conformation (VA; R = AlH_3^-), the



trans-hydroxy-epoxide (and its urethane, above) yielded the *trans*-1 : 4-diol (VII). This result is best explained in terms of an intramolecular process brought about by the $O{\cdot}AlH_3^-$ group in the alternative conformation (VB). The greater ease of the intramolecular reaction * apparently more than offsets the fact that the molecule has to adopt a somewhat less favourable conformation. To a much smaller extent, hydride reduction of the isomeric 2 : 3-epoxy-*trans-cyclo*hexanol also takes place by a similar intramolecular mechanism.[1]

The reaction of the acetate of *cyclo*hex-3-enol (III) with perbenzoic acid was also non-stereospecific, the epoxy-acetate mixture furnishing the *cis*- and the *trans*-1 : 4-diol (29 and 53% respectively as dibenzoates) upon reduction with lithium aluminium hydride.

Experimental

Oxidations were carried out with perbenzoic acid prepared from benzoyl peroxide and sodium methoxide. Care is necessary to ensure that as little methyl benzoate as possible is present in the peracid solution as the b. p. of this ester (~90°/10 mm.) is close to those of some of the epoxides.

Epoxidation of cyclo*Hex*-3-*enol*.—The alcohol (9·3 g.) and perbenzoic acid (0·43 mol.) in ether (300 c.c.) were kept at 0° until reaction was complete (14 days). Calcium hydroxide (40 g.) was added and the mixture was shaken until neutral. After simple distillation from a Claisen flask, the product was distilled fractionally, to give the epoxy-alcohol mixture (9·47 g.), b. p. 99·5—104°/10 mm., n_D^{24} 1·4840—1·4843 (Found: C, 62·8; H, 8·6. Calc. for $C_6H_{10}O_2$: C, 63·15; H, 8·85%). The heterogeneity of the product was shown by conversion of samples of each fraction into a wide-melting α-naphthylurethane (see below).

A much lower yield of epoxide was obtained by washing the reaction solution [from alcohol (4·92 g.) and perbenzoic acid (0·65 mol.) in ether (125 c.c.)] with saturated aqueous potassium hydrogen carbonate solution. The ethereal solution was dried ($MgSO_4$) and evaporated: distillation then gave the epoxy-alcohol mixture (0·61 g.), n_D^{19} 1·4810—1·4842. The aqueous washings were evaporated *in vacuo* and the residue repeatedly extracted with hot ethyl acetate–acetone (3 : 1). Removal of the solvent gave a residue that partially crystallised, and this solid was recrystallised from chloroform–acetone to give the triol (VI; R = H) (2·41 g.), m. p. 123—125°. The remainder of the triol in the mother-liquors was isolated as its *tribenzoate* (8·78 g.), m. p. 155·5—157° (from methanol) (Found: C, 73·0; H, 5·6. $C_{27}H_{24}O_6$ requires C, 72·95; H, 5·45%). The same benzoate was obtained from benzoylation of the pure crystalline triol.

Hydroxylation of cyclo*Hex*-3-*enol and its Benzyl Ether*.—Hydrogen peroxide (7 c.c.; 100-vol.) was added dropwise to a stirred solution of the alcohol (5·15 g.) in 98% formic acid (18·5 g.) at 45—50°. After being stirred for an hour at this temperature the mixture (then homogeneous) was steam-distilled until the distillate was neutral to litmus. The solution was evaporated to

* Cyclic transition states have been proposed for the reduction of certain open-chain halogeno-acids by lithium aluminium hydride.[a]

[a] Eliel and Traxler, *J. Amer. Chem. Soc.*, 1956, **78**, 4049.

dryness and the residue extracted with hot acetone. Concentration and cooling of the acetone extract gave (±)-*cyclo*hexane-1β : 2α : 4β-triol (VI; R = H) (5·86 g.), m. p. 122—125°. Benzoylation afforded the same tribenzoate (m. p. 154—155°) as before.

Similar hydroxylation of 1-benzyloxy*cyclo*hex-3-ene (1·38 g.) in 98% formic acid (3·1 g.) with hydrogen peroxide (1·4 c.c.; 100-vol.) yielded the monobenzyl ether of the triol as a viscous gum. This was dissolved in ethylamine (30 c.c.), finely cut lithium (0·6 g.) was added, and the mixture shaken until the blue colour disappeared (2 hr.). The product isolated by extraction with acetone was benzoylated to give the above tribenzoate (2·67 g.), m. p. 153—155°.

1-*Benzyloxy*cyclo*hex*-3-*ene*.—A mixture of *cyclo*hex-3-enol (10·1 g.), benzyl chloride (50 c.c.), powdered potassium hydroxide (120 g.), and pure dioxan (250 c.c.) was stirred at 50° for 1 hr. After cooling, the solution was treated with water (500 c.c.), and the product isolated with ether. Distillation afforded the *benzyl ether* (18·4 g., 97%), b. p. 78·5—80°/0·5 mm., n_D^{19} 1·5330 (Found: C, 82·8; H, 8·4. $C_{13}H_{16}O$ requires C, 82·95; H, 8·55%).

Lithium Aluminium Hydride Reduction of 3 : 4-*Epoxy*cyclo*hexanol*.—Solutions of the epoxy-alcohol (3·23 g. of combined distillate) in ether (20 c.c.) and lithium aluminium hydride in ether (75 c.c. of 0·4M-solution) were mixed and heated under reflux for 2 hr. Ethyl acetate (50 c.c.) and 2N-sulphuric acid (50 c.c.) were added to the cooled mixture, and the aqueous solution was extracted continuously with ethyl acetate. The crude diol obtained was benzoylated with benzoyl chloride in pyridine at 20°. A cooled solution of the diester in methanol gave *cyclo*hexane-*trans*-1 : 4-diol dibenzoate (4·54 g., 47%), m. p. 140—148° (m. p. 149·6—151° on recrystallisation). The diester from the mother-liquor was distilled in a short-path still at 10^{-5} mm., to give a product that solidified (m. p. 108—115°) at 0°. Recrystallisation from light petroleum (b. p. 80—100°) furnished *cyclo*hexane-*cis*-1 : 4-diol dibenzoate (3·12 g., 34%), m. p. 112·5—114°. Some of the *cis*-dibenzoate was probably lost during the distillation, owing to partial elimination of benzoic acid (which collected as a sublimate).

Formation, Separation, and Reactions of the α-Naphthylurethanes of the Epoxy-alcohols (IV) *and* (V).—The epoxy-alcohol mixture (224 mg.) and α-naphthyl *iso*cyanate (340 mg.) were heated under reflux in light petroleum (b. p. 100—120°) for 20 min. The mixture of derivatives (551 mg.) separated on cooling. This, in light petroleum–benzene (9 : 1), was adsorbed on deactivated alumina (60 g.). Elution with light petroleum–benzene (4 : 1) afforded the *α-naphthylurethane* (286 mg.), m. p. 165—166°, of the *cis*-hydroxy-epoxide (Found: C, 71·9; H, 5·95. $C_{17}H_{17}O_3N$ requires C, 72·05; H, 6·05%). Elution with light petroleum–benzene (7 : 3) afforded the *α-naphthylurethane* (220 mg.), m. p. 146·5—148° (from light petroleum, b. p. 100—120°), of the *trans*-hydroxy-epoxide (Found: C, 72·0; H, 6·05%). Finally elution with ether–methanol (4 : 1) gave the 4-*mono*-*α-naphthylurethane* (39 mg.), m. p. 199·5—200·5° (from acetone–*iso*propyl ether), of the triol (VI) (Found: C, 67·8; H, 6·2. $C_{17}H_{19}O_4N$ requires C, 67·75; H, 6·35%).

The *cis*-α-naphthylurethane (215 mg.) was adsorbed on deactivated alumina (20 g.) as above. After 18 hr. the column was eluted with ether–methanol (4 : 1) to give the triol mono-α-naphthylurethane (178 mg.), m. p. 188—195°. Recrystallisation gave needles, m. p. 199—200°. Similar treatment of the *trans*-α-naphthylurethane (183 mg.) again yielded the triol mono-α-naphthylurethane (41 mg.), m. p. 198·5—200°.

A solution of the *trans*-α-naphthylurethane (507 mg.) and lithium aluminium hydride (1 g.) in tetrahydrofuran (50 c.c.) was heated under reflux for 3 hr. Ethyl acetate and dilute sulphuric acid were added and the diol was isolated by continuous extraction with ethyl acetate. The diol was benzoylated with benzoyl chloride in pyridine; crystallisation of the product from methanol furnished the dibenzoate, m. p. and mixed m. p. 149—151°, of *cyclo*hexane-*trans*-1 : 4-diol (342 mg., 59%).

Epoxidation of 1-*Acetoxy*cyclo*hex*-3-*ene*.—The ester (10·03 g.) and perbenzoic acid in ether (143 c.c.; 0·59M) were mixed and kept at 0° until one mol. of peracid had been consumed. After working up by the calcium hydroxide method, distillation afforded the epoxy-acetate mixture (10·43 g., 95%), b. p. 94—97·5°/10 mm. n_D^{21}, 1·4666—1·4618 (Found: C, 61·3; H, 7·9. Calc. for $C_8H_{12}O_3$: C, 61·5; H, 7·8%).

Part of the epoxy-acetate mixture (3·02 g.) was reduced with lithium aluminium hydride (2 g.) in ether (150 c.c.) as described above for the epoxy-alcohol mixture. Benzoylation of the diol afforded the *trans*-1 : 4-dibenzoate (3·33 g., 53%), m. p. 140—148° (149·5—151° on recrystallisation), and the *cis*-1 : 4-dibenzoate (1·82 g., 29%), m. p. 113—114°.

XUM

The 1-*acetoxy*cyclo*hex*-3-*ene* was prepared in 95% yield from the alcohol (III) (15 g.), acetic anhydride (40 g.), and pyridine (40 g.). It had b. p. 71—72°/20 mm., n_D^{17} 1·4600 (Found: C, 68·2; H, 8·5. $C_8H_{12}O_2$ requires C, 68·55; H, 8·65%).

Epoxidation of cyclo*Hex*-2-*enol*.—The alcohol (4·2 g.) was oxidised with perbenzoic acid (0·45 mol.) in ether (190 c.c.) as described for the βγ-unsaturated alcohol above, calcium hydroxide being used finally to remove acids. The *cis*-hydroxy-epoxide (4·4 g.), b. p. 102—103°/18 mm., n_D^{21} 1·4815, was isolated. The α-*naphthylurethane*, m. p. 173·5—175° [from light petroleum (b. p. 100—120°)], was obtained pure in 91% yield (Found: C, 71·9; H, 5·95. $C_{17}H_{17}O_3N$ requires C, 72·05; H, 6·05%).

Epoxidation of But-3-*enol*.—The alcohol (7·52 g.) was treated with perbenzoic acid as before and the product was isolated by the calcium hydroxide technique. Distillation gave the *epoxide* (6·96 g.), b. p. 80—82°/16 mm., n_D^{22} 1·4397 (Found: C, 54·3; H, 9·2. $C_4H_8O_2$ requires C, 54·55; H, 9·15%).

The authors thank Imperial Chemical Industries Limited for chemicals and the Department of Scientific and Industrial Research for a Maintenance Grant (to B. N.).

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926. *The Preparation and Properties of Aryl 2-Deoxy-α-D-glucopyranosides.*

By F. SHAFIZADEH and M. STACEY.

A number of aryl 2-deoxy-α-D-glucopyranosides have been prepared and their properties investigated. These compounds are less stable towards acidic hydrolysis than the corresponding alkyl derivatives.

A LARGE variety of aryl β-D-glucopyranosides has been prepared through the Koenigs–Knorr [1–3] and the Helferich and Schmitz-Hillebrecht [4] reactions and their properties have been investigated. The corresponding α-anomers, however, are not generally available.[3,5] The Helferich and Schmitz-Hillebrecht reaction, which consists of heating the acetylated sugars with a phenol in presence of an acidic catalyst (toluene-*p*-sulphonic acid or zinc chloride), usually gives an αβ-mixture from which the α-anomer often cannot be isolated.[5] We have found with 1 : 3 : 4 : 6-tetra-*O*-acetyl-2-deoxy-α-D-glucose that this reaction proceeds very readily and provides a variety of aryl 2-deoxy-α-D-glucopyranoside triacetates which can be easily deacetylated by the Zemplén method.[6] The products thus obtained include phenyl 2-deoxy-α-D-glucopyranoside first prepared by Helferich and Iloff [7] by the same method, and other substituted phenyl derivatives used in the following investigations, and listed in Table 4.

The alkaline hydrolysis of phenyl glycosides is facilitated by the anchimeric assistance [8] of a *trans*-hydroxyl group at position 2 and by electron-attracting substituents in the phenyl group. Consequently *p*-nitrophenyl α-D-glucopyranoside is hydrolysed by hot alkaline solutions while the corresponding phenyl derivative shows extreme resistance.[9,10] Treatment of phenyl and *p*-nitrophenyl 2-deoxy-α-D-glucopyranoside with 0·1N-sodium hydroxide at 100° produced a similar result. In the absence of a

[1] Koenigs and Knorr, *Ber.*, 1901, **34**, 957.
[2] Fischer and Mechel, *Ber.*, 1916, **49**, 2813.
[3] Helferich and K.-H. Jung, *Annalen*, 1954, **589**, 77.
[4] Helferich and Schmitz-Hillebrecht, *Ber.*, 1933, **66**, 378.
[5] Bonner, Kubitshek, and Drisko, *J. Amer. Chem. Soc.*, 1952, **74**, 5082.
[6] Zemplén and Pacsu, *Ber.*, 1929, **62**, 1613.
[7] Helferich and Iloff, *Z. physiol. Chem.*, 1933, **221**, 252.
[8] Ballou, *Adv. Carbohydrate Chem.*, 1954, **9**, 59.
[9] Nath and Rydon, *Biochem. J.*, 1954, **57**, 1.
[10] Montgomery, Richtmyer, and Hudson, *J. Amer. Chem. Soc.*, 1943, **65**, 3.

2-hydroxyl group the nitrophenyl glycoside was hydrolysed rapidly, and the corresponding unsubstituted derivative remained unchanged.

The rate of acidic hydrolysis of glycosides is affected by the modification of the carbohydrate moiety as well as by the aglycone group. It has been shown that phenyl glucopyranosides are hydrolysed faster than the corresponding methyl glucopyranosides [11] and, further, the normal glycosides are more stable towards acidic hydrolysis than are the corresponding 2-deoxy-glycosides.[12,13] The rate of hydrolysis of the 2-deoxy-α-D-glucopyranosides with N-hydrogen chloride at 20° (Table 1) reflects the additive effect of these two factors, which results in the rapid acidic hydrolysis of phenyl 2-deoxy-α-D-glucopyranoside.

TABLE 1. *Acidic hydrolysis of 2-deoxy-α-D-glucosides.*

Glycoside	10^4k (sec.$^{-1}$)
Methyl 2-deoxy-α-D-glucopyranoside	2·2
Methyl 2-deoxy-α-D-glucopyranuronoside amide	1·1
p-Aminophenyl 2-deoxy-α-D-glucopyranoside	84·3
Phenyl 2-deoxy-α-D-glucopyranoside	181·6

Detailed investigation of the rate of acidic hydrolysis of other available aryl 2-deoxy-α-D-glucosides was made difficult by their insolubility in cold aqueous acid and their extremely rapid hydrolysis at elevated temperatures. However it was possible to determine the time required for the optical rotation of these compounds to reach a constant value on hydrolysis with 0·001N-hydrochloric acid at 100°. The results (Table 2) indicate the effect of the substituents.

TABLE 2. *Acidic hydrolysis of aryl 2-deoxy-α-D-glucopyranosides.*

Aryl group	(Me)	*p*-NO_2·C_6H_4	*p*-C_6H_4Cl	1-$C_{10}H_7$	*p*-C_6H_4Me	Ph
Time (min.)	(165)	35	15	11	10	6

The above results are in general agreement with those obtained by Nath and Rydon,[9] indicating that, in contrast with the alkaline hydrolysis, the acidic hydrolysis of the phenyl glucosides is facilitated by electron-repelling substituents in the benzene ring.

TABLE 3. *Optical rotation of normal and 2-deoxy-α-D-glucopyranosides.*

	2-Deoxyglucoside			Normal glucoside			Diff.	
Aglycone	$[\alpha]_D$	$[M']_D$	Solv.	$[\alpha]_D$	$[M]_D$	Solv.	$[M]_D - [M']_D$	Ref
Me	135°	24,000°	H_2O	158·9°	30,800°	H_2O	6800	[a]
Et	120	23,200	,,	152	31,800	,,	8600	13, [b]
Ph	161	38,600	MeOH	180·8	46,300	,,	7700	2
p-C_6H_4Me	166	42,200	,,	178	48,100	,,	5900	[a]
p-NH_2·C_6H_4	181	46,200	,,	194·1	52,600	MeOH	6400	[d]
p-NO_2·C_6H_4	210	59,800	,,	215	64,700	H_2O	4900	[a]
			Acetyl derivatives					
Ph	142	52,000	$CHCl_3$	168·7	64,400	$CHCl_3$	12,400	[a]
p-C_6H_4Me	136·6	51,900	MeOH *	162	64,200	,,	12,300	[a]
p-C_6H_4Cl	150	60,100	$CHCl_3$	165·5	69,000	,,	8900	5
p-NO_2·C_6H_4	179	73,600	,,	200	85,400	,,	11,800	[a]

* Not strictly comparable owing to solvent differences.

[a] Hughes, Overend, and Stacey, *J.*, 1949, 2846; Rüber, *Ber.*, 1924, **57**, 1797. [b] Ferguson, *J. Amer. Chem. Soc.*, 1932, **54**, 4086. [c] Nisizawa, *Bull. Chem. Soc. Japan*, 1941, **16**, 155. [d] Goebel, Babers, and Avery, *J. Exp. Med.*, 1932, **55**, 761. [e] Montgomery, Richtmyer, and Hudson, *J. Amer. Chem. Soc.*, 1942, **64**, 690.

In Table 3 the molecular optical rotations of the 2-deoxy-α-D-glucopyranosides are compared with those of the corresponding α-D-glucopyranosides. The difference between each pair is between 4900 and 8600 for the free glycosides and 8900 and 12,400 for the acetylated derivatives. According to the theories of optical rotation [14] these should represent

[11] Heidt and Purves, *J. Amer. Chem. Soc.*, 1944, **66**, 1385.
[12] Overend, Shafizadeh, and Stacey, *J.*, 1950, 671.
[13] Butler, Laland, Overend, and Stacey, *J.*, 1950, 1433.
[14] Whiffen, *Chem. and Ind.*, 1956, 964.

the contribution of the asymmetry at position 2 of the normal glucosides to the total molecular rotation.

Experimental

1 : 3 : 4 : 6-*Tetra*-O-*acetyl*-2-*deoxy*-α-D-*glucose*.—2-Deoxy-D-glucose (7 g.) was added to a mixture of dry pyridine (40 c.c.) and freshly distilled acetic anhydride (25 c.c.) and kept at 0°. After 3 days, when the sugar had completely dissolved, the solution was poured into water and extracted with chloroform. The extract was washed with 1% sulphuric acid, dilute sodium hydrogen carbonate, and finally water. After drying ($MgSO_4$), the solvent was removed by evaporation and the residue evaporated again with absolute alcohol. The syrupy 1 : 3 : 4 : 6-tetra-*O*-acetyl-2-deoxy-α-D-glucose crystallised on trituration with ethanol and was repeatedly recrystallised from the same solvent. In some experiments extraction was eliminated by seeding the aqueous solution and filtering the crystals which separated on storage. The product (8·4 g.) had m. p. 108—109°, $[\alpha]_D^{19}$ +105° (*c* 0·8 in MeOH) (Overend, Stacey, and Stanek [15] give m. p. 91° and $[\alpha]_D^{20}$ +12·3°; Helferich and Iloff [7] give m. p. 109—110°, $[\alpha]_D^{21}$ +109°) (Found: C, 50·8; H, 5·9. Calc. for $C_{14}H_{20}O_9$: C, 50·6; H, 6·1%).

***Phenyl* 2-*Deoxy*-α-D-*glucopyranoside Triacetate*.**—1 : 3 : 4 : 6-Tetra-*O*-acetyl-2-deoxy-α-D-glucose (2·2 g.) and phenol (2 g.) were heated with powdered anhydrous zinc chloride (0·4 g.), with vigorous stirring, at 70° for 35 min. At intervals the acetic acid generated was removed under diminished pressure. The mixture was extracted with benzene (100 c.c.), and the extract filtered, repeatedly washed with 5% sodium hydroxide solution and water, dried ($MgSO_4$), and evaporated to a syrup which crystallised on trituration with ethanol. Recrystallisation from ethanol afforded phenyl 2-deoxy-α-D-glucopyranoside triacetate as large cubes (0·9 g.), m. p. 90°, $[\alpha]_D^{18}$ +141° (*c* 1·12 in MeOH), +142° (*c* 3·58 in $CHCl_3$) (Helferich and Iloff [7] give m. p. 87—88°, $[\alpha]_D^{21}$ +146°) (Found: C, 59·1; H, 6·0. Calc. for $C_{18}H_{22}O_8$: C, 59·0; H, 6·0%).

***Phenyl* 2-*Deoxy*-α-D-*glucopyranoside*.**—Phenyl 2-deoxy-α-D-glucopyranoside triacetate (0·4 g.) was dissolved in dry methanol (25 c.c.), sodium (0·06 g.) was added, and the whole left for 18 hr. at room temperature, then treated with carbon dioxide and evaporated to dryness. The residue was extracted with methanol, and the extract evaporated to a syrup which readily

Table 4. *Aryl 2-deoxy*-α-D-*glucopyranosides.*

No.	2-Deoxy-α-D-glucopyranoside	Yield (%)	Shape	No.	2-Deoxy-α-D-glucopyranoside	Yield (%)	Shape
	Triacetates				*Free glycosides*		
1	*p*-Tolyl	44	Powder	8	*p*-Tolyl	82	Plates
2	*p*-Chlorophenyl	54	Needles	9	*p*-Chlorophenyl	94	Needles
3	*o*-Chlorophenyl	23	Plates	10	*o*-Chlorophenyl	73	Powder
4	*p*-Hydroxyphenyl	9·5	Needles	11	*p*-Nitrophenyl	93	Needles
5	*m*-Hydroxyphenyl	27	Plates	12	α-Naphthyl	89	Needles
6	*p*-Nitrophenyl	37	Needles				
7	α-Naphthyl	31	Conglomerates				

				Found (%)				Required (%)		
No.	M. p.	$[\alpha]_D$ (in MeOH)	Temp.	C	H	N	Formula	C	H	N
1	209—205°	+136·6°	15°	60·0	6·3	—	$C_{13}H_{24}O_8$	60·0	6·3	—
2	133	143	16	53·9	5·2	—	$C_{18}H_{21}O_8Cl$	54·0	5·2	—
3	84—85	109	16	54·1	5·2	—	$C_{18}H_{21}O_8Cl$	54·0	5·2	—
4	154	159	18	56·7	6·0	—	$C_{18}H_{22}O_9$	56·5	5·8	—
5	109—110	126·5	17	56·5	5·4	—	$C_{18}H_{22}O_9$	56·5	5·8	—
6	140—141	170	18	51·7	5·2	3·5%	$C_{18}H_{21}O_{10}N$	52·6	5·1	3·4%
7	85	140	19	63·6	5·7	—	$C_{22}H_{24}O_8$	63·5	5·8	—
8	170	166	19	61·6	6·8	—	$C_{12}H_{16}O_5$	61·5	7·1	—
9	204—205	158	16	52·6	5·3	—	$C_{12}H_{15}O_5Cl$	52·6	5·5	—
10	151—153	123	16	52·0	5·4	—	$C_{12}C_{15}O_5Cl$	52·6	5·5	—
11	173—174	210	19	50·5	5·0	4·7	$C_{12}H_{15}O_7N$	50·5	5·3	4·9
12	157	53·6	19	65·3	6·1	—	$C_{16}H_{18}O_5$	65·1	6·2	—

crystallised. Recrystallisation from ethanol afforded phenyl 2-deoxy-α-D-glucopyranoside as needles (0·21 g.), m. p. 163·5°, $[\alpha]_D^{20}$ +161° (*c* 0·52 in MeOH) {Helferich and Iloff [7] give m. p. 162—163°, $[\alpha]_D$ +159° (in H_2O)} (Found: C, 60·2; H, 6·7. Calc. for $C_{12}H_{16}O_5$: C, 60·0; H, 6·7%).

[15] Overend, Stacey, and Staněk, *J.*, 1949, 2841.

Substituted Phenyl 2-Deoxy-α-D-glucopyranosides.—The compounds listed in Table 4 were prepared essentially by the process described for phenyl 2-deoxy-α-D-glucopyranoside triacetate and its deacetylated product.

p-*Aminophenyl 2-Deoxy-α-D-glucopyranoside.*—*p*-Nitrophenyl 2-deoxy-α-D-glucopyranoside (0·5 g.) in methanol (30 c.c.) was shaken with Raney nickel in an atmosphere of hydrogen. After 2 hr. the reaction was complete. The solution was then filtered and evaporated. Recrystallisation of the residue from methanol–ethyl acetate afforded p-*aminophenyl 2-deoxy-α-D-glucopyranoside* as long plates (0·36 g.), m. p. 179°, $[\alpha]_D$ +181° (*c* 0·54 in MeOH) (Found: C, 55·9; H, 6·8; N, 5·6. $C_{12}H_{17}O_5N$ requires C, 56·5; H, 6·7; N, 5·5%).

Alkaline Hydrolysis of p-*Nitrophenyl 2-Deoxy-α-D-glucopyranoside.*—*p*-Nitrophenyl 2-deoxy-α-D-glucopyranoside (16 mg.) was dissolved in 0·1N-sodium hydroxide (20 c.c.) and kept at 100° under efficient reflux to ensure a constant concentration. At short intervals samples (1 c.c.) were withdrawn, diluted with cold water (9 c.c.), and cooled at 0°. The colour intensity of these light yellowish-green solutions was measured with a Spekker electrophotometer with Ilford filter No. 601. The extent of the hydrolysis was determined by comparing the results with the absorption curve of sodium *p*-nitrophenoxide, previously obtained by measuring a set of standard solution as described by Dyfverman and Lindberg.[16] The results are as follows:

Time (min.)	0	5	10	20	41	60	85	100
Hydrolysis (%)	—	14·4	34·4	54·9	75·1	86·7	98·4	100

Under identical conditions phenyl 2-deoxy-α-D-glucopyranoside remained unaffected and showed a constant optical rotation.

Acid Hydrolysis.—(a) *At room temperature.* Methyl 2-deoxy-α-D-glucopyranuronoside amide, methyl 2-deoxy-α-D-glucopyranoside, phenyl 2-deoxy-α-D-glucopyranoside, and *p*-aminophenyl 2-deoxy-α-D-glucopyranoside were dissolved in N-hydrochloric acid, and their rates of hydrolysis were followed polarimetrically at room temperature (19° ± 1°). The results obtained are summarised in the annexed Tables.

Methyl 2-deoxy-α-D-"glucuronamide" (*c* 0·96)

Time (hr.)	0	6½	18½	51	66	91	120	163	195	384
$[\alpha]_D^{18-20}$	114·5	106	98	77	68·8	58·4	54·2	47·7	43·7	39·5
Hydrolysis (%)	0	11·3	22	50	60·9	74·8	80·4	90	94·4	100

Methyl 2-deoxy-α-D-glucopyranoside (*c* 0·77)

Time (hr.)	0	6	19	27	43	51	66	79	98	268
$[\alpha]_D^{18-20}$	134	118	95	84·4	6·3	61·1	53·2	48	46·8	41·5
Hydrolysis (%)	0	17·4	42·2	53·6	73·1	78·8	87·3	92·9	94·2	100

p-*Aminophenyl 2-deoxy-α-D-glucopyranoside* (*c* 0·27)

Time (min.)	0	30	50	98	145	180	205	380
$[\alpha]_D^{18}$	180	92·6	88·8	59·2	44·5	37	33·3	29·6
Hydrolysis (%)	0	58	60	80	88·3	90	97	100

Phenyl 2-deoxy-α-D-glucopyranoside (*c* 0·27)

Time (min.)	0	6	19	34	45	59	101	136
$[\alpha]_D^{18}$	161	126	85	59	52	44·5	33·4	29·6
Hydrolysis (%)	0	26·5	57·6	77	83	88	96	100

(b) *At* 100°. The glycosides (70 mg.) were dissolved in hot 0·002N-hydrochloric acid (25 c.c.) and kept at 100° under very efficient reflux to ensure a constant volume. At short intervals aliquot parts (2 c.c.) were withdrawn and rapidly cooled at 0°. When hydrolysis was advanced enough to allow the measurement of the optical rotation, without unchanged material crystallising, the rate of hydrolysis was followed polarimetrically to the final constant rotation. The results obtained are given in Table 2.

This investigation was supported by a grant from the British Empire Cancer Campaign (Birmingham Branch).

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[16] Dyfverman and Lindberg, *Acta Chem. Scand.*, 1950, **4**, 878.

XUM

927. *Syntheses of Coronene and* 1 : 2-7 : 8-*Dibenzocoronene.*

By E. Clar and M. Zander.

1 : 12-Benzoperylene-1′ : 2′-dicarboxylic anhydride (II) was obtained in quantitative yield from perylene, maleic anhydride, and chloranil. Decarboxylation gave the hydrocarbon (III) which was condensed to afford coronene-1 : 2-dicarboxylic anhydride (IV) in the same way. Decarboxylation gave coronene in good yield. The tribenzoperylene (VI), condensed with bromomaleic anhydride, afforded the anhydride (VII) which gave 1 : 2-7 : 8-dibenzocoronene on decarboxylation.

The condensation of perylene (I) with maleic anhydride in boiling nitrobenzene as an oxidising agent was described by Clar.[1] We have now obtained quantitative yields of the anhydride (II) by using an excess of boiling maleic anhydride as solvent and chloranil as oxidising agent. Conversion of this anhydride into the hydrocarbon (III) by copper

Fig. 1.

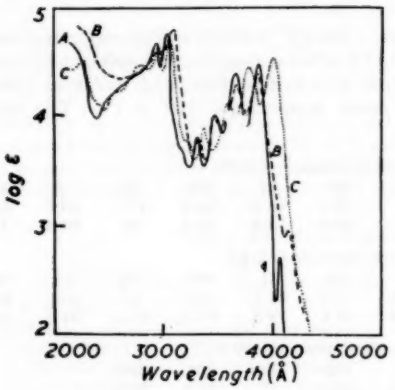


Fig. 2.

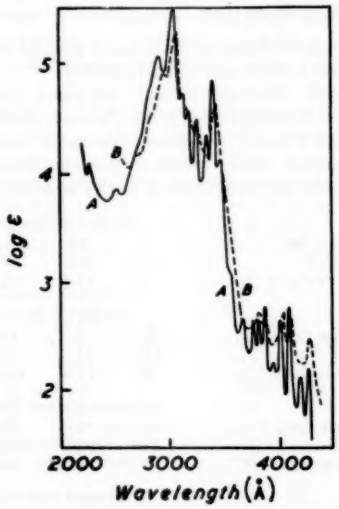


Fig. 1. *Absorption max.* (Å) *and log* ε (*in parentheses*): (*A*) 1 : 12-*benzoperylene* (III) *in* C_6H_6, 4065 (2·75), 3875 (4·45), 3670 (4·40), 3480 (4·02), 3310 (3·80); in EtOH, 3030 (4·75), 2920 (4·65); (*B*) *dipotassium* 1 : 12-*benzoperylene*-1′ : 2′-*dicarboxylate* (*cf.* II) *in* 50% EtOH, 4140 (2·96), 3860 (4·30), 3480 (3·96), 3320 (3·82), 3080 (4·78), 2970 (2·68); (*C*) *dibromo*-1 : 12-*benzoperylene in dioxan*, 4010 (4·54), 3780 (4·46), 3590 (4·13), 3375 (3·91), 3070 (4·73), 2940 (4·62), 2820 (2·48), 2260 (4·52).

Fig. 2. *Absorption max.* (Å) *and log* ε (*in parentheses*): (*A*) *coronene* (V) *in* C_6H_6, 4280 (2·15), 4200 (2·12), 4100 (2·75), 4020 (2·65), 3965 (2·23), 3880 (2·75), 3815 (2·67), 3780 (2·63), 3685 (2·67), 3475 (4·15), 3415 (4·85), 3360 (4·35), 3255 (4·45), 3195 (4·60), 3165 (4·70), 3050 (5·50); *in* EtOH, 2900 (5·10), 2520 (3·88), 2280 (4·08); (*B*) *dipotassium coronene*-1 : 2-*dicarboxylate* (*cf.* IV) *in* 50% EtOH, 4300 (2·47), 4120 (2·63), 4060 (2·71), 3900 (2·61), 3830 (2·70), 3430 (4·67), 3280 (4·41), 3070 (5·027), 2950 (4·89).

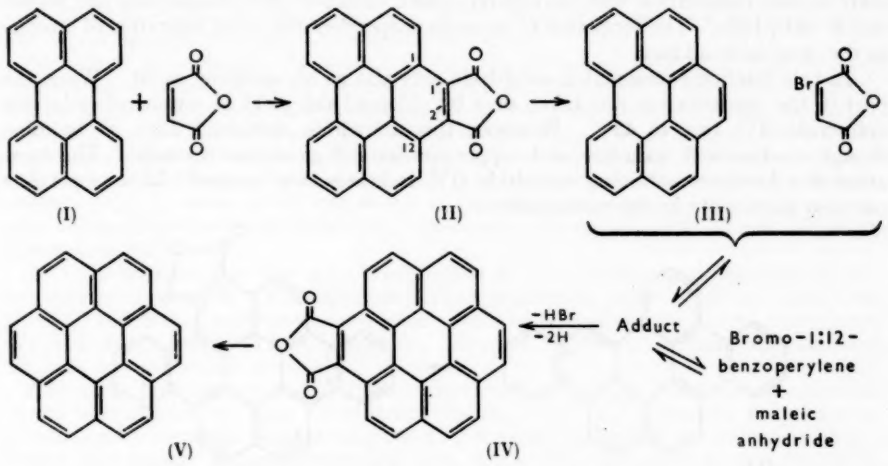
powder in quinoline is very slow, requiring several days: better results were obtained by sublimation with soda-lime in a vacuum.

It has been reported that 1 : 12-benzoperylene (III) could not be further condensed with maleic anhydride in boiling nitrobenzene.[1] However, this condensation to coronene-1 : 2-dicarboxylic anhydride (IV) was easily achieved by the modification just mentioned, and coronene was easily obtained by decarboxylation. The overall yield being 25% from

[1] Clar, *Ber.*, 1932, **65**, 846.

commercial perylene and 41% from 1 : 12-benzoperylene, this is the simplest and most efficient synthesis of coronene.

The above results can be best explained by assumption of a dissociable adduct of



perylene or 1 : 12-benzoperylene and maleic anhydride which precedes the dehydrogenation to the aromatic anhydrides (II) or (IV). This is supported by the application of bromomaleic anhydride, instead of maleic anhydride, in the case of 1 : 12-benzoperylene.

FIG. 3.

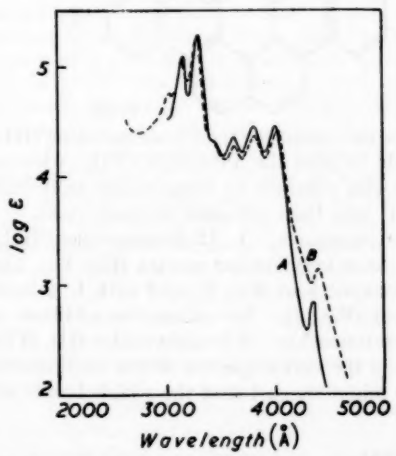


FIG. 4.

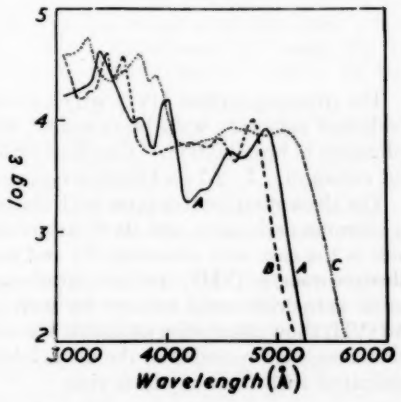
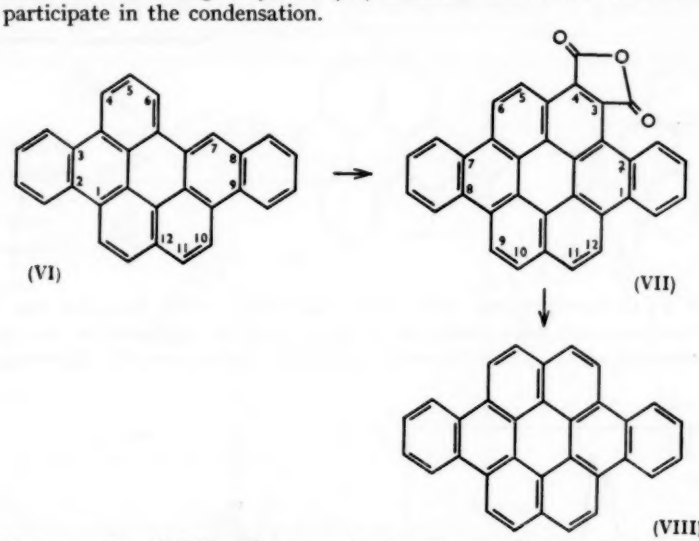


FIG. 3. *Absorption max.* (Å) *and log* ε (*in parentheses*): (*A*) 1 : 2-7 : 8-*dibenzocoronene* (VIII) *in* $C_6H_3Cl_3$, 4350 (2·84), 4010 (4·46), 3810 (4·44), 3630 (4·32), 3300 (5·29), 3160 (5·07); (*B*) *dipotassium* 1 : 2-7 : 8-*dibenzocoronene*-5 : 6-*dicarboxylate* (*cf.* VII) *in* 50% EtOH, 4380 (3·17), 4020 (4·42), 3820 (4·38), 3635 (4·28), 3280 (5·30), 3150 (5·01), 3030 (4·73).

FIG. 4. *Absorption max.* (Å) *and log* ε (*in parentheses*): (*A*) 1 : 12-*benzoperylene*-1′ : 2′-*dicarboxylic anhydride* (II) *in* $C_6H_3Cl_3$, 4880 (3·88), 4575 (3·72), 4000 (4·18), 3775 (4·02), 3400 (4·62); (*B*) *coronene*-1 : 2-*dicarboxylic anhydride* (IV) *in* $C_6H_3Cl_3$, 4780 (3·99), 4470 (3·82), 4230 (3·81), 3620 (4·58), 3460 (4·59), 3080 (4·54); (*C*) 1 : 2-7 : 8-*dibenzocoronene*-5 : 6-*dicarboxylic anhydride* (VII) *in* $C_6H_3Cl_3$, 5050 (3·91), 4610 (3·93), 3900 (4·41), 3750 (4·59), 3290 (3·73).

The dissociation of this adduct could lead to bromobenzoperylene and maleic anhydride. In fact, this reaction gave only 20% (% of product) of alkali-soluble and 80% of alkali-insoluble product. The latter consisted mainly of a uniform crystalline dibromo-1 : 12-benzoperylene, which could have been formed only by the repetition of the assumed addition and dissociation with the initial product, bromo-1 : 12-benzoperylene and bromomaleic anhydride. The formation of bromobenzoperylenes involves migration of bromine in the dissociable adduct.

In this reaction bromomaleic anhydride acts also as an oxidising agent. When this part in the condensation was taken over by chloranil the yield of coronenedicarboxylic anhydride (IV) rose to 43%. However, this anhydride contained 3·5% of bromine, though reaction with soda-lime and copper powder still gave pure coronene. The formation of a bromine-containing anhydride (IV) indicates that bromo-1 : 12-benzoperylene can also participate in the condensation.



(VI) (VII) (VIII)

The tribenzoperylene [2] (VI), which proved to be more reactive than benzoperylene (III), condensed smoothly with bromomaleic anhydride to give the anhydride (VII), with no indication of bromination. Excellent yields were also obtained by using maleic anhydride and chloranil. 1 : 2-7 : 8-Dibenzocoronene (VIII) was then obtained in good yield.

The absorption spectra agree with the presumed structures. 1 : 12-Benzoperylene (III), its dibromo-derivative, and its dicarboxylic acid have very similar spectra (Fig. 1). The same is the case with coronene (V) and its dicarboxylic acid (Fig. 2), and with 1 : 2-7 : 8-dibenzocoronene (VIII) and its dicarboxylic acid (Fig. 3). No endocyclic addition of maleic anhydride could account for such a close relationship. The anhydrides (II), (IV), and (VII) show absorption at similar wavelengths in the visible spectra, whilst considerable differences were recorded in the ultraviolet: this might suggest that the visible bands are associated with the anhydride ring.

Experimental

M.p.s were taken in evacuated capillaries. Microanalyses are by Mr. J. M. Cameron and Miss M. W. Christie.

1 : 12-*Benzoperylene*-1′ : 2′-*dicarboxylic anhydride* (II).—Commercial perylene (Shore Transit Company Ltd., 80 Wolmer Gardens, Edgware, Middlesex) (10 g.) was dissolved in boiling maleic anhydride (150 g.), and chloranil (21 g.) added in portions. The red brown anhydride crystallised almost immediately. After 10 minutes' refluxing, hot xylene (200 ml.) was added, the

[2] Clar, *Chem. Ber.*, 1949, **82**, 53.

warm mixture was filtered, and the red brown needles (12·8 g.) were washed with xylene and ether.

1 : 12-*Benzoperylene* (III).—Benzoperylenedicarboxylic anhydride (5·5 g.) and soda-lime (16·5 g.) were powdered together and heated at 350° for 1 hr. The sublimation-apparatus was evacuated (0·02 mm.) and the temperature raised to 440° for 9½ hr. The sublimate (2·7 g.) recrystallised from xylene in large plates, m. p. 273°.[1] With copper powder in boiling quinoline only 10% of the anhydride was decarboxylated in 2 days.

Coronene-1 : 2-*dicarboxylic Anhydride* (IV).—(*a*) 1 : 12-Benzoperylene (2 g.) and chloranil (7·2 g.) in maleic anhydride (20 g.) were refluxed for 5 hr. Hydrogen chloride was evolved and dark red needles crystallised from the hot mixture. Warm nitrobenzene (30 ml.) was added, the suspension was cooled to about 70°, and the needles (2 g.) were filtered off, washed with nitrobenzene and ether, and further purified by extraction with boiling nitrobenzene (50 ml.) (1·7 g.), vacuum-sublimation, and crystallisation from nitrobenzene. The orange-red needles of *anhydride* began to sinter at 455° and melted at 490—503° with decomposition. Hot concentrated sulphuric acid dissolved them with a yellow colour (Found: C, 84·2; H, 2·5. $C_{26}H_{10}O_3$ requires C, 84·3; H, 2·7%).

(*b*) 1 : 12-Benzoperylene (0·5 g.), chloranil (0·44 g.), and bromomaleic anhydride (8 ml.) were refluxed for 75 min. The anhydride (IV) crystallised in needles (0·29 g.) which were filtered off and washed with benzene and ether. After two recrystallisations from nitrobenzene the anhydride still contained 3·5% of bromine. However, it gave pure coronene when sublimed with soda-lime and copper powder.

Dibromo-1 : 12-*benzoperylene*.—1 : 12-Benzoperylene (10 g.) and bromomaleic anhydride (70 ml.) were refluxed for 1 hr. After cooling, xylene (50 ml.) was added and the precipitate filtered off and washed with benzene and ether. Extraction with dilute hot sodium hydroxide solution gave impure coronenedicarboxylic acid (2 g.). The residue (8 g.) was repeatedly extracted with boiling xylene, and the extract treated with charcoal, filtered, and concentrated. *Dibromo*-1 : 12-*benzoperylene* separated in yellow needles. These were chromatographed in benzene on activated alumina. They then melted at 260—262° and dissolved in hot concentrated sulphuric acid to a red-violet solution (Found: C, 60·8; H, 2·6; Br, 36·8. $C_{22}H_{10}Br_2$ requires C, 60·9; H, 2·3; Br, 36·8%).

Coronene (V).—Coronene-1 : 2-dicarboxylic anhydride (0·3 g.) and soda-lime (1 g.) were ground together and heated under nitrogen to 400° for 45 min. The sublimation-apparatus was evacuated and the temperature raised to 420° for 2 hr. Coronene sublimed in pale yellow needles (0·16 g.). Recrystallised from xylene it had m. p. and mixed m. p. 425—428°. Hot sulphuric acid dissolved it with a yellowish-green colour. Decarboxylation could also be effected by prolonged boiling with quinoline and copper powder (Found: C, 96·1; H, 4·2; Calc. for $C_{24}H_{12}$: C, 96·0; H, 4·0%).

1 : 2-7 : 8-*Dibenzocoronene*-3 : 4-*dicarboxylic Anhydride* (VII).—(*a*) 1 : 12-2 : 3-8 : 9-Tribenzoperylene [2] (VI) (2 g.) was refluxed in bromomaleic anhydride (40 ml.) for 2 hr. The *anhydride* (VII) which crystallised was filtered off and washed with nitrobenzene and ether, boiled with 1-methylnaphthalene (200 ml.) (to remove any starting material), filtered off (1·5 g.), and recrystallised from nitrobenzene as dark violet needles which sintered at 395°, decomposed at 440—450°, and dissolved in concentrated sulphuric acid to a brown-yellow solution (Found: C, 86·5; H, 2·9. $C_{34}H_{14}O_3$ requires C, 86·8; H, 3·0%).

(*b*) Tribenzoperylene (VI) (0·2 g.), chloranil (0·5 g.), and maleic anhydride (5 g.) were refluxed for 90 min. The mixture was diluted with warm nitrobenzene, and the anhydride (0·22 g.) filtered off and washed with nitrobenzene and ether. Purification as above yielded an identical product.

1 : 2-7 : 8-*Dibenzocoronene* (VIII).—The anhydride (VII) (0·3 g.) and soda-lime (1 g.) were ground together and heated to 350° under nitrogen for 45 min. Sublimation was carried out at 430—450°/0·08 mm. during 4 hr. The sublimate (0·13 g.) was recrystallised from 1-methylnaphthalene and resublimed in a vacuum. 1 : 2-7 : 8-*Dibenzocoronene* formed yellow needles, m. p. 496—499°, which dissolved in hot concentrated sulphuric acid to a blue-violet solution (Found: C, 95·9; H, 4·2. $C_{32}H_{16}$ requires C, 96·0; H, 4·0%).

One of us (M. Z.) is indebted to Rütgerswerke A.G., Frankfurt/Main, for a scholarship.

UNIVERSITY OF GLASGOW. [*Received, May 21st,* 1957.]

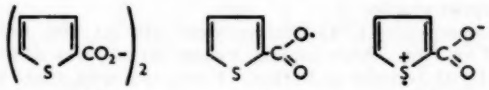
XUM

928. *Decomposition Reactions of Heterocyclic Diacyl Peroxides. Part II.*[1] *2-Thenoyl Peroxide.*

By M. C. Ford and Donald Mackay.

The compounds formed by the decomposition of 2-thenoyl peroxide (I) in aromatic solvents can be attributed largely to reactions of 2-thenoyloxy-radicals (II). The most regular feature was the production of aryl 2-thenoates, in small yield, by nuclear attack, and in the halogenobenzenes phenyl 2-thenoate was formed, with displacement of the halogen. In toluene and cumene attack occurred preferentially in the side-chain. In solvents lacking side-chain hydrogen, the formation of 2-thenoic anhydride was sometimes observed. In thiophen, 2-thienyl 2-thenoate and 2 : 2′-dithienyl were produced, the latter providing evidence for the generation of 2-thienyl radicals.

Breitenbach and Karlinger[2a] showed that 2-thenoyl peroxide (I) was an efficient initiator for the polymerisation of styrene. We have now studied the decomposition of this peroxide in various aromatic solvents. In benzene, nitrobenzene, chlorobenzene,



(I) (II) (III)

bromobenzene, and iodobenzene, much amorphous material containing combined sulphur was produced, but moderate amounts (0·6—0·9 mole per mole of peroxide) of 2-thenoic acid were formed, together with poor yields of simple neutral products. In a *ca.* 50% solution of naphthalene in benzene a smoother reaction occurred, the naphthalene being attacked preferentially. In toluene and cumene there were very marked increases in the yields both of the acid (1·4 and 2·0 moles respectively) and of simple neutral products, and no complex material was formed. Carbon dioxide estimations showed the production of 0·26 mole in benzene and 0·17 mole in toluene, and in neither solvent was thiophen found among the final products.

In benzene phenyl 2-thenoate was formed, in the naphthalene–benzene mixture 1-naphthyl 2-thenoate, and in nitrobenzene (in minute yield) *p*-nitrophenyl 2-thenoate. Attack *para* to the substituent in the benzene ring was also observed with both chlorobenzene and bromobenzene, *p*-chlorophenyl and *p*-bromophenyl 2-thenoates being produced. But in these last two solvents the chief product was *phenyl* 2-thenoate, and this ester was again formed when the peroxide was decomposed in iodobenzene. Its production from the halogenobenzenes must have involved attack at the carbon atom already bearing the halogen: in iodobenzene free iodine was liberated, and in bromobenzene hydrogen bromide was evolved; in chlorobenzene combined chlorine was detected in the intractable residues. Considerable amounts of 2-thenoic anhydride were isolated from the decomposition reactions in benzene and chlorobenzene, and smaller amounts in iodobenzene, and in chlorobenzene a little 2-thienyl 2-thenoate was produced.

In toluene substantial amounts of dibenzyl were formed, together with smaller quantities of tolyl 2-thenoates (mainly the *o*-isomer), benzyl 2-thenoate, and 2-benzylthiophen; an acid, $C_{10}H_6O_4S_2$, believed to be 5-2′-thenoyloxy-2-thenoic acid was also isolated in small yield. In cumene, where the yield of 2-thenoic acid indicated exclusive side-chain attack, dicumyl was the only neutral product isolated.

[1] *J.*, 1951, 824, is to be regarded as Part I of this series.

[2] Breitenbach and Karlinger, *Sitzungsber. Akad. Wiss. Wien*, (*a*) 1951, **160** (IIB), 304; (*b*) 1949, **158** (IIB), 739.

The pattern of the decomposition reactions in toluene (reactions 1—3) clearly shows that the peroxide generates 2-thenoyloxy-radicals ($\theta\cdot CO_2\cdot$):

$$\theta\cdot CO_2\cdot + Ph\cdot CH_3 \longrightarrow \theta\cdot CO_2H + Ph\cdot CH_2\cdot \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$2Ph\cdot CH_2\cdot \longrightarrow (Ph\cdot CH_2\cdot)_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$\theta\cdot CO_2\cdot + Ph\cdot CH_2\cdot \longrightarrow \theta\cdot CO_2\cdot CH_2Ph \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

The thenoyloxythenoic acid apparently arises either by their attack upon 2-thenoic acid or by a self-interaction process. The analogous 4-1′-naphthoyloxy-1-naphthoic acid is produced when 1-naphthoyl peroxide is decomposed in carbon tetrachloride.[3] The scanty evolution of carbon dioxide and the formation of only small amounts of a product, 2-benzylthiophen, attributable to 2-thienyl radicals ($\theta\cdot$) indicate that the thenoyloxy-radicals are rather stable (probably on account of mesomerism: II ⟷ III), undergoing decarboxylation to only a moderate extent, and the preferential formation of the side-chain products shows that they react typically by hydrogen abstraction, and less readily by nuclear attack.

The reactive nature of the thiophen nucleus present in the substrate probably accounts for the low yields of simple neutral products obtained in solvents lacking easily abstractable hydrogen: the relatively large amounts of 2-thenoic acid formed in these solvents probably arise mainly by hydrogen-transfer processes involving the accumulating complex material (cf. Part I).

The acyloxylations and the halogen displacements were of considerable interest, for acyloxylation of simple aromatic solvents by a diacyl peroxide generally occurs to a negligible extent: only " reactive " substrates (*e.g.*, naphthalene [4] and anthracene [5]) are benzoyloxylated by benzoyl peroxide, simple aromatic solvents being phenylated; the halogen displacements appear to resemble those brought about by chlorine atoms, which displace bromine from aryl bromides, with the formation of aryl chlorides.[6]

The production of 2-thenoic anhydride in three of the first group of solvents, though not in toluene or cumene, suggested that there could be a process, competing with homolytic fission, in which the peroxide was directly reduced (cf. the formation of benzoic anhydride from benzoyl peroxide in the oxidation of triphenylphosphine to triphenylphosphine oxide [7]) and that the accumulating complex sulphur-containing material might be responsible. This view was strengthened by showing that ethyl sulphide also reduced the peroxide to the anhydride; benzoyl peroxide was similarly reduced to benzoic anhydride. Decomposition of 2-thenoyl peroxide in thiophen gave no anhydride; instead, 2-thienyl 2-thenoate was produced in good yield, together with smaller amounts of 2 : 2′-dithienyl. The decomposition of benzoyl peroxide in thiophen likewise gave 2-thienyl benzoate.

The formation of 2-benzylthiophen in toluene and of 2 : 2′-dithienyl in thiophen can be attributed to reactions of 2-thienyl radicals. Strong competition by solute molecules is probably responsible for their apparent inability to thienylate the aromatic solvents (cf. phenylation with benzoyl peroxide): for example, hydrogen-transfer processes would lead to thiophen, which would be subject to further attack; the benzylthiophen formed in toluene probably arises in this way, rather than by the direct union of thienyl with benzyl radicals; an independent experiment showed that benzyl radicals (generated [8] by the interaction of *tert.*-butyl peroxide and toluene) attacked thiophen, and that 2-benzyl-thiophen was the product. In the affinity it shows for benzyl and acyloxy-radicals thiophen in fact resembles a substrate such as anthracene,[8,5] and differs from a typical aromatic solvent.

[3] Kharasch and Dannley, *J. Org. Chem.*, 1945, **10**, 406.
[4] Boyland and Sims, *J.*, 1953, 2966.
[5] Roitt and Waters, *J.*, 1952, 2695.
[6] Voegtli, Muhr, and Läuger, *Helv. Chim. Acta*, 1954, **37**, 1627.
[7] Challenger and Wilson, *J.*, 1927, 209; Greenbaum, Denney, and Hoffmann, *J. Amer. Chem. Soc.*, 1956, **78**, 2563.
[8] Beckwith and Waters, *J.*, 1957, 1001.

Experimental

Solvents.—" AnalaR " benzene was dried over sodium; toluene, thiophen, and ethyl sulphide were fractionated over sodium. Cumene was purified as described by Hey *et al.*[9] Nitrobenzene was fractionated under reduced pressure. Chlorobenzene and bromobenzene were fractionated and stored over sodium hydroxide. Iodobenzene was shaken with silver powder and redistilled under reduced pressure.

Esters of 2-Thenoic Acid.—Treatment of 2-thenoic acid,[10] m. p. 127—128°, with thionyl chloride gave an almost quantitative yield of the acid chloride, b. p. 77°/10 mm. The following esters (prisms) were prepared under Schotten–Baumann conditions from the appropriate phenol, 2-hydroxythiophen being obtained as described by Hurd and Kreuz:[11] ***phenyl***, m. p. 54° (Found: C, 64·5; H, 4·05; S, 15·3. $C_{11}H_8O_2S$ requires C, 64·7; H, 3·95; S, 15·7%), **1-*naphthyl***, m. p. 80° (Found: C, 70·6; H, 4·05; S, 12·2. $C_{15}H_{10}O_2S$ requires C, 70·8; H, 4·0; S, 12·6%), p-***chlorophenyl***, m. p. 84—84·5° (Found: C, 55·2; H, 3·1; Cl, 14·9. $C_{11}H_7O_2ClS$ requires C, 55·35; H, 3·0; Cl, 14·9%), p-***bromophenyl***, m. p. 85° (Found: C, 46·4; H, 2·7; Br, 28·5. $C_{11}H_7O_2BrS$ requires C, 46·65; H, 2·5; Br, 28·2%), and ***2-thienyl 2-thenoate***, straw-coloured, m. p. 54° (Found: C, 51·6; H, 2·9. $C_9H_6O_2S_2$ requires C, 51·4; H, 2·9%) (all from light petroleum; b. p. 50—60°). The phenyl ester had been prepared by Rhodehamal and Degering,[12] who, however, recorded neither analytical data nor a m. p. p-***Nitrophenyl 2-thenoate***, prepared in pyridine solution, formed needles, m. p. 181°, from methanol (Found: C, 52·8; H, 2·9; N, 5·4. $C_{11}H_7O_4NS$ requires C, 53·0; H, 2·8; N, 5·6%).

2-Thenoyl Peroxide (I).—2-Thenoyl chloride (14 g.) in *cyclo*hexane (20 ml.) was added to a cooled (ice–salt) mixture of 2N-sodium hydroxide (40 ml.) and aqueous hydrogen peroxide (30 vol.; 50 ml.) with vigorous mechanical stirring: the crystalline peroxide separated immediately. Stirring was continued for 15 min. and the product was then collected and dried ***in vacuo***. Recrystallisation from benzene by addition of light petroleum (b. p. 30—40°), gave dense colourless prisms (60—65%), m. p. 103° (sharp, with subsequent decomp.) [Found : equiv. (iodometric), 126. Calc. for $C_{10}H_6O_4S_2$: equiv., 127]; Breitenbach and Karlinger [2b] record m. p. 92—93° (decomp.).

Decompositions in Aromatic Solvents.—The decompositions in benzene, the halogenobenzenes, and nitrobenzene were carried out in the dark, and an oil-bath was used as the source of heat, for with these solvents the presence of light or the occurrence of superheating led to excessive tar-formation.

Working up consisted in removal of the solvent under reduced pressure (the last traces of nitrobenzene and iodobenzene were eliminated by steam-distillation), followed by extraction of the residue with ether (insoluble polymer being removed at this stage) and separation of the 2-thenoic acid by repeated shaking with 2N-potassium hydrogen carbonate. Except in the case of the toluene decomposition, the acid was obtained pure after recrystallisation from water. After drying ($MgSO_4$) of the ethereal solution the ether was removed and the neutral residue then treated as described.

Benzene. The peroxide (6·0 g.) was decomposed in benzene (600 ml.) at 75—85° for 48 hr. under nitrogen: 0·26 mole of carbon dioxide per mole of peroxide was evolved (sorption on soda-asbestos). The solvent was removed and the resulting tar extracted with boiling ether; the insoluble residue (0·7 g.), which could be precipitated as a brown amorphous powder (Found: S, 21·3%) from benzene solution by addition of methanol, was not further investigated. The ethereal solution gave 2-thenoic acid (1·9 g.) and neutral material, which when distilled at 0·01 mm. yielded an oil (0·7 g.); chromatography of this on anhydrous magnesium sulphate from light petroleum (b. p. 50—60°) gave phenyl 2-thenoate (0·2 g.), m. p. and mixed m. p. 53° after recrystallisation from light petroleum (Found: C, 64·9; H, 4·0; S, 15·3%), and 2-thenoic anhydride (0·3 g.), m. p. 60·5—61·5° (from light petroleum) (Found: C, 50·5; H, 2·5. Calc. for $C_{10}H_6O_3S_2$: C, 50·4; H, 2·5%), identical with an authentic specimen.[13]

In another experiment the peroxide (750 mg.) was decomposed in benzene (75 ml.) for 24 hr. and the solvent was distilled through a short column. A portion of the distillate was shaken

[9] Hey, Pengilly, and Williams, *J.*, 1956, 1463.
[10] Hartough, " Thiophene and its Derivatives," Interscience Publ. Inc., New York, 1952, pp. 503, 505.
[11] Hurd and Kreuz, *J. Amer. Chem. Soc.*, 1950, **72**, 5543.
[12] Rhodehamal and Degering, *J. Amer. Pharm. Assoc.*, 1942, **31**, 281.
[13] Steinkopf and Ohse, *Annalen*, 1924, **437**, 19.

with isatin in concentrated sulphuric acid: the colour response, when compared with that given by standard solutions of thiophen in benzene, showed that the reaction mixture contained <1 mg. of thiophen.

Naphthalene–benzene. The peroxide (1·0 g.) was added to a solution of naphthalene (20 g.) in benzene (20 ml.) at 50° and the whole heated at 80—90° for 10 hr. The mixture gave 2-thenoic acid (0·54 g.) and a gum, which was digested with hot light petroleum (b. p. 50—60°). The petroleum solution was chromatographed on magnesium sulphate; trituration of the eluted oil with light petroleum gave crystals (0·1 g.), which after two recrystallisations from light petroleum afforded 1-naphthyl 2-thenoate, m. p. and mixed m. p. 80°, strongly depressed in admixture with naphthalene.

Nitrobenzene. Decomposition of the peroxide (12 g.) in nitrobenzene (1180 ml.) at 85—95° for 36 hr. gave 2-thenoic acid (2·7 g.) and a dark product, which on trituration with methanol yielded a coloured solid (50 mg.); two recrystallisations from methanol (charcoal) gave *p*-nitrophenyl 2-thenoate, m. p. and mixed m. p. 179—180°.

Chlorobenzene. Decomposition of the peroxide (18 g.) in chlorobenzene (1620 ml.) at 65—75° for 45 hr. gave 2-thenoic acid (6·5 g.) and neutral material, which was distilled at 0·01 mm.: chromatography of the distillate on magnesium sulphate from light petroleum (b. p. 50—60°) solution afforded two oily fractions, A (1·4 g.) and B (1·4 g.).

Fraction A was chromatographed on Norit from light petroleum (b. p. 60—70°); elution with chloroform–light petroleum (1 : 9) gave phenyl 2-thenoate (0·38 g.); recrystallised from light petroleum (b. p. 30—40°) it had m. p. and mixed m. p. 53° (Found: C, 64·9; H, 4·0%). Further elution, with chloroform–light petroleum (2 : 3), gave, in turn, *p*-chlorophenyl 2-thenoate (0·02 g.), m. p. and mixed m. p. 82—83° (from ether–light petroleum), and 2-thienyl 2-thenoate (0·17 g.), m. p. and mixed m. p. 53° (from light petroleum).

Fraction B was obtained crystalline by re-chromatographing it on magnesium sulphate from light petroleum (b. p. 50—60°); recrystallised from light petroleum it had m. p. 59·5°, undepressed in admixture with 2-thenoic anhydride.

In a similar experiment, in which the peroxide (9·0 g., 36 mmoles) gave 0·24 g. (1·2 mmoles) of the phenyl ester, the total combined chlorine (in the crude carboxylic acid and the involatile residues) was found to amount to 0·11 g. (3×10^{-3} g.-atom).

Bromobenzene. (*a*) Decomposition of the peroxide (15 g.) in bromobenzene (1400 ml.) at 75—80° for 24 hr. gave 2-thenoic acid (6·9 g.) and a dark gum, which was distilled at 0·01 mm.; chromatography of the oily distillate on Norit, with chloroform–light petroleum mixtures, gave phenyl 2-thenoate (0·17 g.) and *p*-bromophenyl 2-thenoate (0·26 g.), m. p. 83° (from methanol): the mixed m. p. with an authentic sample was 84—85°.

(*b*) A solution of the peroxide (7 g., 28 mmoles) in bromobenzene (100 ml.) was introduced, during 3 hr., into boiling bromobenzene (500 ml.) through which dry nitrogen was passed, and the effluent gases were bubbled through acidified silver nitrate. The mixture was then refluxed for a further hour, the current of nitrogen being maintained. Silver bromide (0·40 g., 2·1 mmoles) collected in the trap. The mixture, worked up as in (*a*), gave the carboxylic acid (2·6 g.), the phenyl ester (0·57 g., 2·8 mmoles), and a trace of the *p*-bromophenyl ester.

Iodobenzene. A solution of the peroxide (2·5 g., 10 mmoles) in iodobenzene (60 ml.) was added all at once, with vigorous shaking, to iodobenzene (190 ml.) at 150°; the whole was then heated at 150° for 5 min. and cooled. The mixture was deep red, owing to liberation of iodine (1×10^{-3} g.-atom), which was determined by repeated extraction with saturated aqueous potassium iodide and titration of the combined extracts with 0·1N-thiosulphate. The organic layer gave 2-thenoic acid (0·9 g.) and neutral material, which was distilled at 0·05 mm. Chromatography of the distillate on Norit, in the usual way, gave phenyl 2-thenoate (0·12 g., 0·6 mmole), m. p. and mixed m. p. 53°, and a solid (30 mg.) which on recrystallisation (twice) from light petroleum yielded 2-thenoic anhydride, m. p. and mixed m. p. 60—61°.

Toluene. The peroxide (18 g.) was decomposed in toluene (1700 ml.) at 75—85° under nitrogen for 48 hr.; 0·17 mole of carbon dioxide per mole of peroxide was evolved. The acidic material (12·5 g.) obtained, which had a melting-range of 105—110°, was digested with boiling water: the soluble fraction was shown (by sublimation of a portion) to contain 11·0 g. of pure 2-thenoic acid. Trituration of the insoluble fraction with aqueous methanol yielded 5(?)-2′-*thenoyloxy-2-thenoic acid* (0·17 g.) as prisms, m. p. 195° (decomp.) (Found: C, 47·3; H, 2·2. $C_{10}H_6O_4S_2$ requires C, 47·2; H, 2·4%); with diazomethane it gave the *methyl ester*, which formed prisms, m. p. 131—132° (decomp.), from light petroleum (b. p. 60—70°) (Found: C,

49·4; H, 3·3. $C_{11}H_8O_4S_2$ requires C, 49·2; H, 3·0%). Hydrolysis of the acyloxy-acid furnished 2-thenoic acid, together with a highly soluble hydroxythenoic acid, which with aqueous ferric chloride gave an intense vermilion colour, rapidly changing to a dark red precipitate.

The residue from the organic layer was distilled at 0·01 mm., giving two fractions: A (4·5 g.), b. p. 70—80°, which crystallised on cooling, and B (1·5 g.), b. p. 100—150°. Fraction A on recrystallisation from methanol gave dibenzyl, m. p. and mixed m. p. 48—50°. The mother-liquor was evaporated and the residue chromatographed on alumina from light petroleum (b. p. 30—40°); further dibenzyl (2·9 g. in all) was obtained, along with 2-benzylthiophen, which was characterised by conversion into 2-benzyl-5-chloromercurithiophen (0·16 g.), prisms, m. p. and mixed m. p. 184—185° (lit.,[14] 189—191°), from methanol–chloroform (Found: C, 32·5; H, 2·5. Calc. for $C_{11}H_9SHgCl$: C, 32·1; H, 2·2%).

Fraction B was refluxed with potassium hydroxide (4 g.) in alcohol (25 ml.) for 30 min. The alcohol was removed, and water (20 ml.) added: ether-extraction gave an oil (0·4 g.), identified as benzyl alcohol (phenylcarbamate, m. p. and mixed m. p. 76—77°). The alkaline solution yielded 2-thenoic acid (0·7 g.), again purified by sublimation, and phenolic material (0·2 g.); treatment of the latter with α-naphthyl *iso*cyanate gave slightly impure *o*-tolyl α-naphthylcarbamate, m. p. 136° after recrystallisation from light petroleum (b. p. 60—70°), which did not depress the m. p. of an authentic sample, m. p. 142°, and strongly depressed the m. p.s of authentic samples of the *m*- and the *p*-isomer.

In another experiment (1·0 g. of peroxide in 95 ml. of toluene) the effluent nitrogen was passed through a trap at −70°; the solvent was finally distilled through a column at atmospheric pressure, the first runnings being added to the condensate in the trap; the mixture was shown to contain <0·2 mg. of thiophen.

Cumene. Decomposition of the peroxide (3·0 g.) in cumene (300 ml.) at 70—80° under nitrogen for 36 hr. gave 2-thenoic acid (3·0 g.) and a pale yellow oil, which was distilled at 0·6 mm. Chromatography of the distillate (1·2 g.) from light petroleum (b. p. 50—60°) afforded dicumyl (2 : 3-dimethyl-2 : 3-diphenylbutane) (0·24 g.), m. p. and mixed m. p. 117°, after recrystallisation from methanol.

Decomposition of Peroxides in Thiophen.—(a) *2-Thenoyl peroxide.* A solution of the peroxide (3·0 g.) in thiophen (100 ml.) was refluxed for 16 hr. The thiophen was removed, the residue was taken up in ether, and 2-thenoic acid (1·3 g.) was extracted. The organic layer was then evaporated and distilled at 0·02 mm. Trituration of the distillate (1·0 g.) with light petroleum (b. p. 30—40°) gave 2-thienyl 2-thenoate (0·50 g.). The petroleum-soluble fraction was chromatographed on magnesium sulphate, yielding 2 : 2′-dithienyl (0·12 g.), obtained as plates, m. p. 34—35°, from methanol, identical with an authentic sample,[11] m. p. 34°, and a further quantity of the ester (0·73 g. in all), m. p. and mixed m. p. 53°, after recrystallisation from light petroleum (b. p. 30—40°).

(b) *Benzoyl peroxide.* A solution of the peroxide (4·0 g.) in thiophen (100 ml.) was refluxed for 24 hr. The thiophen was removed and the residue taken up in ether. Benzoic acid (2·6 g.) was obtained by extraction, and the ether layer was evaporated and distilled at 1 mm. The distillate (0·9 g.) was chromatographed (twice) on magnesium sulphate from light petroleum (b. p. 30—40°) solution, yielding 2-thienyl benzoate [11] (0·51 g.), nodules (from light petroleum), m. p. and mixed m. p. 43—44°.

Reduction of Peroxides with Ethyl Sulphide.—(a) *2-Thenoyl peroxide.* The peroxide (3·0 g.) was added in small portions to the sulphide (6 g.); the reaction was exothermic and external cooling (ice) was necessary. The colourless solution was refluxed for 3 min. and concentrated, and gave 2-thenoic acid (1·9 g.); the neutral residue (1·0 g.) on trituration with light petroleum (b. p. 30—40°) gave 2-thenoic anhydride (0·63 g.), m. p. and mixed m. p. 59—60° (from light petroleum).

(b) *Benzoyl peroxide.* In a similar experiment, with benzoyl peroxide (8·0 g.) and ethyl sulphide (16 g.), benzoic acid (5·0 g.) and benzoic anhydride (1·3 g.) were obtained. The latter was purified by chromatography on magnesium sulphate, and had m. p. and mixed m. p. 43°, after recrystallisation from ether–light petroleum.

In neither case was any attempt made to isolate the oxidation products of the sulphide, or other neutral compounds.

Decomposition of tert.*-Butyl Peroxide in Toluene–Thiophen.*—The peroxide (10 g.), toluene

[14] Steinkopf, *Annalen*, 1921, **424**, 54.

(50 ml.), and thiophen (50 ml.) were refluxed together for 7 days. Concentration of the reaction mixture at atmospheric pressure left a high-boiling residue, which was extracted with light petroleum (b. p. 30—40°); the extract on evaporation and distillation at 10 mm. gave 2-benzylthiophen (0·5 g.), identified by conversion into its 5-chloromercuri-derivative. No dibenzyl was formed.

We are indebted to Dr. E. C. Kooyman for helpful discussions. One of us (D. M.) also thanks the Carnegie Trust for the Universities of Scotland for a scholarship, and the Murdo Macaulay Trust for a grant. Micro-analyses are by Miss D. A. Thomson and Dr. R. A. Chalmers.

THE UNIVERSITY, OLD ABERDEEN. [*Received, June 12th*, 1957.]

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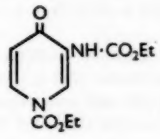
929. *Oxazolopyridines and Oxazoloquinolines. Part II.* Synthesis of 2′-Hydroxyoxazolo(4′ : 5′-2 : 3)pyridine and Related Compounds.*

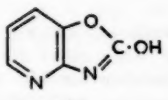
By JAMES FRASER and E. TITTENSOR.

The synthesis of 2′-hydroxyoxazolo(4′ : 5′-2 : 3)pyridine (II), and attempted synthesis of 2′-hydroxyoxazolo(4′ : 5′-3 : 4)pyridine are described. Oxazolo(4′ : 5′-3 : 4)quinoline was obtained by cyclising 3-formamido-4-hydroxyquinoline with phosphoryl chloride, but this method failed to give unsubstituted oxazolopyridines.

2′-HYDROXYOXAZOLO(4′ : 5′-3 : 4)PYRIDINE could not be obtained by heating 3-amino-4-hydroxypyridine hydrochloride with urea, the only product isolated being 4-hydroxy-3-pyridylurea, a result which was similar to that observed in the quinoline series.[1] For a possible alternative route 3-amino-4-hydroxypyridine was treated in pyridine with ethyl chloroformate, readily giving the bisethoxycarbonyl derivative (I), but not the required monoethoxycarbonyl compound, even when an excess of the amine was used. The pyridone (I) was converted by cold aqueous sodium hydroxide into the urethane (IV), which was heated to 200° (cf. Groenvik [2]), but the expected hydroxyoxazole could not be isolated.



(I)



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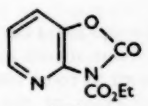
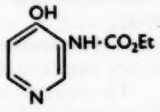


(III)



(IV)

It was of interest to ascertain whether the isomeric hydroxyoxazole (II) could be obtained by a similar series of reactions from 2-amino-3-hydroxypyridine, the hydroxyl group of which should be more phenolic [3] than that of 3-amino-4-hydroxypyridine. Ethyl chloroformate with 2-amino-3-hydroxypyridine in pyridine gave 2-ethoxycarbonylamino-3-pyridyl ethyl carbonate, which was converted by aqueous sodium hydroxide into 2-ethoxycarbonylamino-3-hydroxypyridine. The expected hydroxyoxazole (II) was obtained by heating the latter to 200° in diphenyl ether.

* Part I, *J.*, 1956, 1781.

[1] Bachman, Welton, Jenkins, and Christian, *J. Amer. Chem. Soc.*, 1947, **69**, 365.
[2] Groenvik, *Bull. Soc. chim.*, 1876, **25**, 178.
[3] Elderfield, "Chemistry of Heterocyclic Compounds," John Wiley and Sons, Inc., New York, 1950, Vol. I, p. 442.

In contrast with the behaviour of the pyridone (I), which was unchanged at 200° in inert solvents, 2-ethoxycarbonylamino-3-pyridyl ethyl carbonate on vacuum-distillation gave the ethoxycarbonyloxazolone (III) together with a little hydroxyoxazole (II), into which the oxazolone (III) was converted by cold, dilute sodium hydroxide solution.

Since 2-amino-3-hydroxypyridine with benzoic anhydride gave 2′-phenyloxazolo-(4′ : 5′-2 : 3)pyridine,[4] an attempt was made to prepare the unsubstituted oxazolopyridines by refluxing 2-formamido-3- and 3-formamido-4-hydroxypyridine with phosphoryl chloride: this failed, although oxazolo(4′ : 5′-3 : 4)quinoline was obtained in low yield by this method.

Experimental

4-Hydroxy-3-pyridylurea.—3-Amino-4-hydroxypyridine hydrochloride (2·6 g.) was fused with urea (3 g.) at 140—150° for 2 hr., allowed to cool, and triturated with water to remove urea. The product was filtered off and crystallised from water, giving the *pyridylurea* (2·3 g.), m. p. 300—302° (decomp.), sintering at 270° (Found: C, 47·0; H, 4·9; N, 27·8. $C_6H_7O_2N_3$ requires C, 47·1; H, 4·6; N, 27·4%).

1-Ethoxycarbonyl-3-ethoxycarbonylamino-4-pyridone (I).—A solution of 3-amino-4-hydroxypyridine (2·2 g., 0·02 mole) in pyridine (8 c.c.) was cooled to 0° and ethyl chloroformate (4·3 g., 0·04 mole) was added dropwise with stirring. The mixture was kept overnight at room temperature, then 5N-hydrochloric acid was added to give a pH of 4. After 30 min. at 0° the precipitate was collected and washed with a little water. Crystallisation from aqueous alcohol gave the *pyridone* (3·4 g.), m. p. 83·5—84·5° (Found: C, 52·0; H, 5·5; N, 11·1. $C_{11}H_{14}O_5N_2$ requires C, 52·0; H, 5·5; N, 11·0%).

3-Ethoxycarbonylamino-4-hydroxypyridine (IV).—1-Ethoxycarbonyl-3-ethoxycarbonylamino-4-pyridone (1 g.) was dissolved in N-sodium hydroxide (6 c.c.), and after 2 min. at room temperature the solution was neutralised with N-hydrochloric acid (vigorous evolution of carbon dioxide). The mixture was evaporated to dryness under reduced pressure and the residue was extracted with hot chloroform. Concentration of the filtered extract gave *3-ethoxycarbonylamino-4-hydroxypyridine* as needles, m. p. 148—149° (Found: C, 52·6; H, 5·7; N, 15·6. $C_8H_{10}O_3N_2$ requires C, 52·7; H, 5·5; N, 15·4%).

2-Amino-3-hydroxypyridine.[5]—A mixture of 3-hydroxy-2-nitropyridine (10 g.), methanol (100 c.c.), and 10% palladised charcoal (1 g.) was shaken with hydrogen at 1 atm. until absorption ceased. Removal of the catalyst and evaporation under reduced pressure in an atmosphere of nitrogen gave the brown product (6·9 g.) which was used without further purification. A specimen for analysis (m. p. 163—165°) was obtained by crystallisation (charcoal) from acetone–chloroform (Found: C, 54·3; H, 5·1; N, 25·8. Calc. for $C_5H_6ON_2$: C, 54·5; H, 5·5; N, 25·5%).

2-Ethoxycarbonylamino-3-pyridyl Ethyl Carbonate.—A solution of 2-amino-3-hydroxypyridine (1·6 g.) in dry pyridine (4 c.c.) was stirred at 0° while ethyl chloroformate (3·2 g.) was added dropwise. The mixture was kept at room temperature for 3 hr. and the pH was adjusted to 4 with hydrochloric acid. Extraction of the mixture with ether, evaporation of the dried (Na_2SO_4) extract, and keeping the residue in a vacuum-desiccator over concentrated sulphuric acid for several hours gave crude 2-ethoxycarbonylamino-3-pyridyl ethyl carbonate as a brown viscous oil (3·1 g.).

2-Ethoxycarbonylamino-3-hydroxypyridine.—Crude 2-ethoxycarbonylamino-3-pyridyl ethyl carbonate (3 g.) was warmed on a steam-bath with N-sodium hydroxide (20 c.c.) for 5 min. and allowed to cool, and the excess of oil was removed by extraction with ether. After a further 10 min. at room temperature the mixture was neutralised with dilute hydrochloric acid and evaporated to dryness under reduced pressure. The residue was extracted with hot chloroform, evaporation of which gave the crude urethane as a sticky solid (1 g.). This was recrystallised several times from chloroform–ether, affording *2-ethoxycarbonylamino-3-hydroxypyridine* as light yellow prisms, m. p. 104—105° (Found: N, 15·6. $C_8H_{10}O_3N_2$ requires N, 15·4%).

2′-Hydroxyoxazolo(4′ : 5′-2 : 3)pyridine (II).—2-Ethoxycarbonylamino-3-hydroxypyridine (0·4 g.) was heated in diphenyl ether (3 c.c.) at 200° for 1 min. and, after cooling, treated with

[4] Fraser and Tittensor, *J.*, 1956, 1781.
[5] B.P. 360,188/1931; Bray, Neale, and Thorpe, *Biochem. J.*, 1950, **46**, 506.

light petroleum (b. p. 60—80°; 3 c.c.). The solid was collected and dissolved in acetone–chloroform (1 : 1), and the solution was clarified by filtration through kieselguhr. Concentration of the filtrate gave the *oxazolopyridine* (0·1 g.), m. p. 211—212° (Found: C, 53·1; H, 3·0; N, 20·9. $C_6H_4O_2N_2$ requires C, 52·9; H, 2·9; N, 20·6%). The *picrate* formed yellow prisms, m. p. 154—155°, from benzene (Found: C, 39·0; H, 1·9. $C_6H_4O_2N_2,C_6H_3O_7N_3$ requires C, 39·5; H, 1·9%).

3′-Ethoxycarbonyl-2′-oxo-oxazolo(4′ : 5′-2 : 3)pyridine (III).—Crude 2-ethoxycarbonylamino-3-pyridyl ethyl carbonate (2·4 g.) was distilled at 2 mm. The distillate solidified and was recrystallised from ether–light petroleum (b. p. 40—60°), giving *3′-ethoxycarbonyl-2′-oxo-oxazolo(4′ : 5′-2 : 3)pyridine* (0·79 g.) as needles, m. p. 105—106·5° (Found: C, 51·7; H, 3·9; N, 13·6. $C_9H_8O_4N_2$ requires C, 51·9; H, 3·8; N, 13·5%).

The tarry distillation residue was extracted with acetone–benzene (1 : 1), and the solution was treated with charcoal and filtered through kieselguhr. The filtrate on concentration gave colourless needles (0·05 g.), m. p. alone or mixed with 2′-hydroxyoxazolo(4′ : 5′-2 : 3)pyridine 211—212°.

Decomposition of the Oxazolone (III) *in Alkaline Solution.*—The oxazolone (0·1 g.) was stirred with N-sodium hydroxide (0·6 c.c.) until dissolution was complete (5 min.). After a further 2 min. the solution was neutralised with N-sulphuric acid (0·6 c.c.) (evolution of carbon dioxide). The solution gradually deposited a colourless solid which was collected and recrystallised from acetone–benzene, giving 2′-hydroxyoxazolo(4′ : 5′-2 : 3)pyridine, m. p. and mixed m. p. 211—212°.

Attempted Cyclisation of 1-Ethoxycarbonyl-3-ethoxycarbonylamino-4-pyridone (I).—Liquid paraffin (2 c.c.) was heated to 200° and the pyridone (0·1 g.) was added. Heating was continued for 3 min. and the mixture was cooled and treated with light petroleum (b. p. 40—60°; 5 c.c.). A colourless precipitate was obtained, together with a small amount of a red resin. The precipitate was collected and washed with light petroleum. It (0·05 g.) had m. p., alone or mixed with starting material, 83·5—84·5°.

2′-Phenyloxazolo(4′ : 5′-2 : 3)pyridine.—2-Amino-3-hydroxypyridine (1 g.) was refluxed with benzoic anhydride (6 g.) for 10 min. The cooled mixture was dissolved in benzene (200 c.c.) and extracted with ice-cold 3N-hydrochloric acid (3 × 20 c.c.). The combined extracts were filtered and basified with aqueous sodium hydroxide. The precipitate was collected and crystallised from aqueous acetone, giving the *2′-phenyl derivative* as needles, m. p. 127—127·5° (Found: C, 73·2; H, 4·0; N, 14·5. $C_{12}H_8ON_2$ requires C, 73·4; H, 4·1; N, 14·3%).

Oxazolo(4′ : 5′-3 : 4)quinoline.—Crude, dry 3-formamido-4-hydroxyquinoline (0·5 g.), obtained from 3-amino-4-hydroxyquinoline and formic acid, was refluxed with phosphoryl chloride (2 c.c.) for 1 hr. Crushed ice (20 g.) and ammonia (*d* 0·880; 25 c.c.) were added and the mixture was immediately extracted with benzene (3 × 20 c.c.). The dried (Na_2SO_4) extract was distilled to remove benzene, and the residue was crystallised from light petroleum (b. p. 40—60°). The *oxazole* formed pale yellow needles (0·05 g.), m. p. 105—105·5° (Found: C, 70·0; H, 3·8; N, 16·5. $C_{10}H_6ON_2$ requires C, 70·6; H, 3·5; N, 16·5%).

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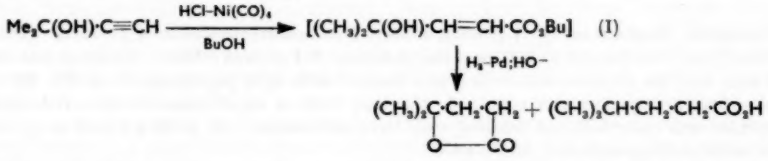
[*Received, June 18th,* 1957.]

930. *Researches on Acetylenic Compounds. Part LVII.* A General Synthesis of Allenic Acids.*

By E. R. H. Jones, G. H. Whitham, and M. C. Whiting.

The reaction between 2-methylbut-3-yn-2-ol, nickel carbonyl, and hydrogen chloride gives the ester of a conjugated allenic acid as the main product and involves the corresponding acetylenic chloride as an intermediate. Analogous chlorides of widely varying substitution patterns react similarly with nickel carbonyl, giving a range of allenic acids by a simple and convenient procedure.

Parts XXII [1] and XXIX [2] of the present Series describe the reactions of nickel carbonyl with mono- and di-substituted acetylenes, respectively, from a preparative standpoint, while Parts XXX [3] and XXXI [4] discuss the stoicheiometry of the reaction and some complexities (inhibition and catalysis) of its mechanism. Bergmann and Zimkin [5] have described a reaction between 2-methylbut-3-yn-2-ol, nickel carbonyl, anhydrous butanol, and hydrogen chloride, which was formulated as follows:



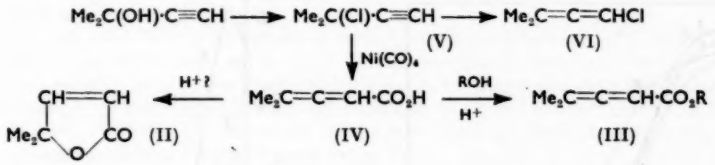
The main fraction of the reaction mixture was a heterogeneous liquid believed to be essentially the ester (I). It was hydrogenated over palladium, then hydrolysed, separation of acidic and neutral products giving γ-methylvalerolactone and γ-methylvaleric acid in unstated yields. *Prima facie* evidence was thus adduced for a reversal, under these conditions, of the direction of addition of H · · · CO_2H to the acetylenic bond proved by Reppe *et al.*[6] for simple monosubstituted acetylenes and assumed in Part XXII of this Series.[1] To clarify the situation it was necessary to find which of the changes in molecular structure and reaction conditions were responsible for this reversal, particularly since some features reported by Bergmann and Zimkin were ambiguous or unexpected. The evidence for the primary product (I) was inconclusive, especially since the postulated hydrogenolysis over palladium is inconsistent with the work of Haynes and Jones.[7]

The experiment was therefore repeated essentially as described; a main fraction was obtained with physical constants close to those reported. On careful fractional distillation two homogeneous substances were separated (from appreciable amounts of higher-boiling materials of still unknown constitution) and identified as the known lactone (II), and the allenic ester (III). The latter was hydrolysed to the crystalline acid (IV), of which the structure follows from ultraviolet and infrared spectra, hydrogenation to γ-methylvaleric acid, and the production of acetone on ozonolysis. There is thus no need to assume the formation of the ester (I), since the hydrogenation products isolated by Bergmann and Zimkin were obviously derived from our products (II) and (III); indeed even the heterogeneous higher-boiling fractions could not have contained their ester (I) in quantity.

* Part LVI, *J.*, 1957, 2597.

[1] Jones, Shen, and Whiting, *J.*, 1950, 230.
[2] *Idem*, *J.*, 1951, 48.
[3] *Idem*, *J.*, 1951, 763.
[4] *Idem*, *J.*, 1951, 766.
[5] Bergmann and Zimkin, *J.*, 1950, 3455.
[6] Reppe (and his collaborators), *Annalen*, 1953, **582**, 1.
[7] Haynes and Jones, *J.*, 1946, 954.

Further investigation showed that 2-methylbut-3-yn-2-ol is probably not directly involved in the reaction with nickel carbonyl. In the reaction conditions used, it would be converted rapidly (if reversibly) into the chloride (V); just possibly this might be isomerised to the allene (VI) in the presence of nickel chloride.[8] These chlorides were therefore prepared and treated with nickel carbonyl in aqueous-methanolic acetic acid. The allene (VI) failed to react, but (V) gave the ester (III; R = Et) in fair yield. When sodium acetate was added in excess so that nickel chloride, a Lewis acid and an efficient esterification catalyst, could not be formed, the free acid (IV) was the main product. The neutral fraction contained the ester (III; R = Et) and a small quantity of lactone (II); the yield of the latter was much smaller than in the original experiment starting with 2-methylbut-3-yn-2-ol. We believe that the reason for the difference in the yield-ratio for the lactone and allenic acid derivative is trivial rather than fundamental, *i.e.*, that the former is formed from the allenic acid under the catalytic action of the acidic species present, rather than that the alcohol itself is involved in a reaction with nickel carbonyl, leading directly to the lactone. This view is supported indirectly by the isomerisation of 2-butylbuta-2 : 3-dienoic acid (see below) to the lactone of 2-butyl-4-hydroxybut-2-enoic acid when an attempt was made to distil a sample *in vacuo*.



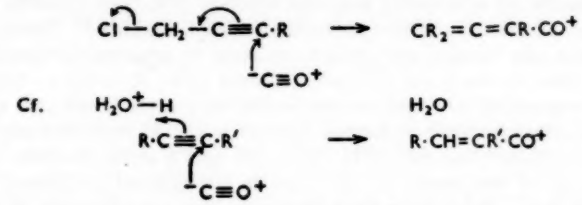
Under Bergmann and Zimkin's conditions, 1-ethynyl*cyclo*hexanol, prop-2-yn-1-ol, and 1 : 1-diphenylprop-2-yn-1-ol failed to give significant quantities of isolable reaction products with nickel carbonyl, although the last alcohol was converted into a non-crystalline and undistillable deeply coloured syrup, from which no acidic compound was obtained on hydrolysis. 3-Methylpent-1-yn-3-ol, on the other hand, underwent a reaction analogous to that of its lower homologue. This is the only alcohol of the four which readily yields a chloride on treatment with hydrogen chloride.

As a route to an allenic acid, the reaction of a chloride of the type (V) with nickel carbonyl in buffered aqueous ethanol compares favourably with the alternative method described by Wotiz,[9] in which the derived Grignard reagent is treated with carbon dioxide and the resulting $\beta\gamma$-acetylenic and $\alpha\beta\gamma$-allenic acids and a dimeric acid are separated, although with some experimental difficulty. The general reaction is: $R^1{\cdot}C{\equiv}C{\cdot}CR^2R^3Cl \longrightarrow HO_2C{\cdot}CR^1{:}CR^2R^3$, and several variants were therefore investigated in addition to the case $R^1 = H$, $R^2 = R^3 = Me$, described above. Six chlorides (with $R^1 = R^2 = R^3 = H$; $R^1 = R^2 = H$, $R^3 = Me$; $R^1 = R^2 = H$, $R^3 = Pr^n$; $R^1 = R^2 = H$, $R^3 = Ph$; $R^1 = Bu$, $R^2 = R^3 = H$; and $R^1 = Bu$, $R^2 = R^3 = Me$) gave the corresponding allenic acids, although in some cases yields were low, probably because isolation procedures were insufficiently mild for these somewhat unstable compounds. The method is thus general, and it renders $\alpha\beta\gamma$-allenic acids as accessible as many more familiar conjugated dienes; in view of their great reactivity [10] they may be useful synthetical intermediates. The crystalline penta-2 : 3-dienoic acid thus obtained is one of the simplest possible resolvable allenes; its participation in prototropic rearrangements has already been discussed.[11]

Like the normal Reppe carboxylation, this variant can be written as a nucleophilic

[8] Hennion, Sheehan, and Maloney, *J. Amer. Chem. Soc.*, 1950, **72**, 3542.
[9] Wotiz, *ibid.*, 1950, **72**, 1639.
[10] See, *inter al.*, Eglinton, Jones, Mansfield, and Whiting, *J.*, 1954, 3197.
[11] Jones, Whitham, and Whiting, *J.*, 1954, 3201.

addition of the $^{-}C{\equiv}O^{+}$ fragment, concerted in this case with displacement of Cl^{-} instead of addition of H^{+}:



In both reactions, however, it seems probable that the breakdown of an unstable metal complex involving carbon monoxide and the acetylene is involved; recently several such complexes have been described for other transition metals.[12] The stoicheiometry of this new

FIG. 1. (1) *Buta-2 : 3-dienoic acid*; (2) *penta-2 : 3-dienoic acid*; (3) *4-methylpenta-2 : 3-dienoic acid*; (4) *2-butylbuta-2 : 3-dienoic acid.*

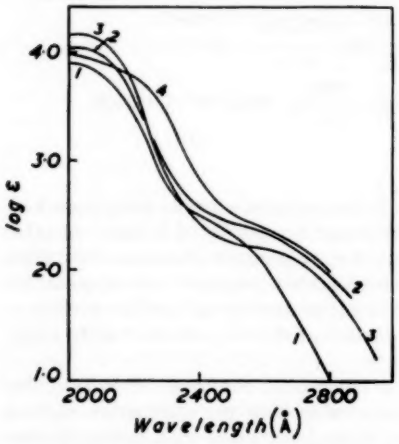
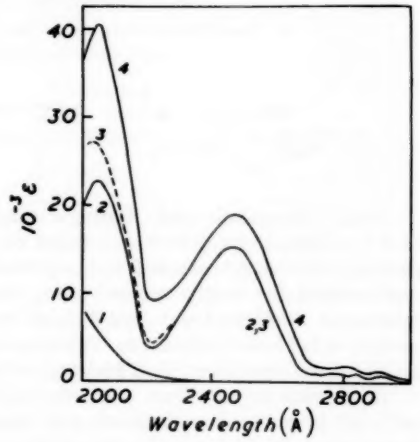


FIG. 2. (1) *Acrylic acid*; (2) *styrene*; (3) *summation curve for* 1 + 2; (4) *4-phenylbuta-2 : 3-dienoic acid.*



variant has been investigated in a preliminary manner only. No acid is required (though acetic acid was in fact present in most of the experiments described), and the molar ratio $[Ni(CO)_4]$: [Chloride] : [Cl^{-} formed] : [Allenic acid derivative] appears to be roughly 2 : 2 : 2 : 1.

The ultraviolet absorption spectra of the allenic acids further confirm the simple generalisation of Celmer and Solomons [13] about allenes, that the two fragments separated by the central carbon atom of the allene grouping behave approximately as though insulated from each other. This is shown in Fig. 1 in the case of the simple αβγ-allenic acids which, like αβ-ethylenic acids, have a marked inflexion at about 2400—2600 Å, and in Fig. 2 for 4-phenylbuta-2 : 3-dienoic acid. In the latter the absorption of the allene is very similar to, but 30—50% more intense than, the sum of the curves for acrylic acid and styrene. Much of the vibrational fine-structure (benzenoid spacing of *ca.* 900 cm.$^{-1}$) in the spectrum of styrene is lost on passing to the allenic acid. Some qualification of the above generalisation is thus necessary.

The infrared spectra of allenic acids and esters have already been discussed by Wotiz

[12] Reppe and Vetter, *Annalen*, 1953, **582**, 133; Sternberg, Greenfield, Friedel, Wotiz, Markby, and Wenders, *J. Amer. Chem. Soc.*, 1954, **76**, 1457.
[13] Celmer and Solomons, *ibid.*, 1953, **75**, 1372.

and Celmer,[14] with whose findings our results for the substances now described are in agreement. The intense doublet at about 1920 and 1970 cm.$^{-1}$ is a characteristic feature of acids of the type $H_2C{=}C{=}CR{\cdot}CO_2H$ and their derivatives; acids of types $R{\cdot}CH{=}C{=}CH{\cdot}CO_2H$ and $R_2C{=}C{=}CR{\cdot}CO_2H$ show a single band at 1960—1970 cm.$^{-1}$. An intense band at 850 cm.$^{-1}$ is observed in all compounds $R_2C{=}C{=}CH_2$, and is presumably attributable to the olefinic C–H out-of-plane deformation mode, which occurs at *ca.* 890 cm.$^{-1}$ in $R_2C{=}CH_2$.

Experimental

Reaction between Nickel Carbonyl and 2-Methylbut-3-yn-2-ol.—A mixture of butan-1-ol (150 c.c., containing hydrogen chloride, 40 g.) and 2-methylbut-3-yn-2-ol (84 g.) was stirred under nitrogen and warmed to 40° while nickel carbonyl (44 c.c.) was added dropwise during 2 hr. at such a rate as to maintain the temperature at about 65°. After cooling and removal of excess of nickel carbonyl by co-distillation with ether (100 c.c.) the residue was poured into water and extracted with ether. The acid fraction yielded an oil (0·5 g.) which solidified and crystallised from water as fine needles (0·13 g.), m. p. 59° (Found: C, 61·25; H, 8·6%; equiv., 209). Light absorption max. at 2210 Å ($E^{1\%}_{1\,cm.}$ 430). This acid was not investigated further. Careful distillation of the neutral fraction gave, after removal of butanol, homogeneous fractions: (i) (18·5 g.), b. p. 85—86·5°/12 mm., n_D^{20} 1·4443, and (ii) (32 g.), b. p. 64·5—65°/0·1 mm., n_D^{19} 1·4600, together with heterogeneous fractions of higher b. p.

Fraction (i) was identified as 4-hydroxy-4-methylpent-2-enoic lactone (17% yield) (Haynes and Jones [7] give b. p. 80°/10 mm., n_D^{18} 1·4470). Hydrogenation in ethyl acetate over platinum resulted in the uptake of 98% of the theoretical amount of hydrogen and gave the corresponding saturated lactone, b. p. 105° (bath)/16 mm., n_D^{20} 1·4249, m. p. *ca.* 2° (Noyes [15] gives b. p. 208°/760 mm., m. p. 7—8°), identified by conversion into 4-hydroxy-4-methylpentanamide, m. p. 99—101°, with aqueous ammonia (Ström [16] gives m. p. 101°).

Fraction (ii) was set aside for 7 days at 15° in 10% aqueous methanolic potassium hydroxide (300 c.c.). Dilution with water followed by extraction with ether and careful distillation of the extract gave butanol. The acid fraction solidified slowly; crystallisation from light petroleum (b. p. 40—60°) gave *4-methylpenta-2 : 3-dienoic acid* as small prisms (8·2 g., 7·5% overall), m. p. 80—85°, raised to 89—90° on two further recrystallisations (Found: C, 64·5; H, 7·35%; equiv., 109. $C_6H_8O_2$ requires C, 64·3; H, 7·2%; equiv., 112).

Hydrogenation (0·97 mol.) in ethyl acetate over platinum yielded γ-methylvaleric acid, b. p. 103—105° (bath-temp.)/7 mm., n_D^{15} 1·4181 (Homnelen [17] gives b. p. 199°/752 mm., n_D^{20} 1·4144), identified by conversion into the amide, m. p. 117·5—119·5° (from benzene–light petroleum) (Homnelen [17] gives m. p. 118·5°).

A slow stream of ozonised oxygen was passed through a solution of the acid (0·61 g.) in acetic acid (40 c.c.) at 18° and the emergent gases were washed by passing through a water trap. The water and acetic acid solutions were combined, zinc dust (4 g.) was added, and the mixture distilled in steam. Addition of aqueous 2 : 4-dinitrophenylhydrazine sulphate solution yielded, after three recrystallisations from ethanol, the 2 : 4-dinitrophenylhydrazone of acetone (0·77 g., 60%), m. p. and mixed m. p. 126—127°.

Reaction between Nickel Carbonyl and 3-Methylpent-1-yn-3-ol.—A mixture of dry butanol (80 g.), hydrogen chloride (20 g.), and 3-methylpent-1-yn-3-ol (49 g.) was treated with nickel carbonyl as above. The neutral fraction was isolated with ether, most of the butanol was removed by distillation at atmospheric pressure, and the residue was partially purified by distillation, yielding a pale yellow liquid (36 g.), b. p. 40—60°/0·1 mm. This was hydrolysed with 10% aqueous-ethanolic potassium hydroxide (400 c.c.) at 20° for 5 days; the solution was then acidified and extracted and the extract separated into neutral and acid fractions. Distillation of the former gave *4-hydroxy-4-methylhex-2-enoic lactone* (10·1 g., 16%), b. p. 104—105°/17 mm., n_D^{24} 1·4485 (Found: C, 66·7; H, 8·3. $C_7H_{10}O_2$ requires C, 66·6; H, 8·0%). The latter, on distillation, yielded *4-methylhexa-2 : 3-dienoic acid* (11·6 g., 18%), b. p. 92—94°/0·05 mm., n_D^{20} 1·4731 (Found: C, 66·0; H, 7·95%; equiv., 131. $C_7H_{10}O_2$ requires C, 66·6; H, 8·0%; equiv., 126).

[14] Wotiz and Celmer, *J. Amer. Chem. Soc.*, 1952, **74**, 1860.
[15] Noyes, *ibid.*, 1901, **23**, 395.
[16] Ström, *J. prakt. Chem.*, 1893, **48**, 419.
[17] Homnelen, *Bull. Soc. chim. belges*, 1933, **42**, 243.

Ethyl 4-Methylpenta-2 : 3-dienoate.—3-Chloro-3-methylbut-1-yne (11 g.) in ethanol (40 c.c.), acetic acid (6 c.c.), and water (1·5 c.c.) was treated with nickel carbonyl (4 c.c.) at 40°. Removal of excess nickel carbonyl, isolation with ether, and separation of the negligible acid fraction left a residue which was distilled, giving ethyl 4-methylpenta-2 : 3-dienoate (3·1 g., 22%), b. p. 99—102°/60 mm., n_D^{18} 1·4580. Alkaline hydrolysis for 20 hr. at 20° gave the acid, m. p. 89—90°, in *ca.* 70% yield.

4-Methylpenta-2 : 3-dienoic Acid (preferred method).—3-Chloro-3-methylbut-1-yne (10·3 g.) was added slowly to a stirred solution of sodium acetate (16 g.), acetic acid (12 g.—probably unnecessary), water (3 c.c.), and nickel carbonyl (15 c.c.) at 40° during 30 min.; a mildly exothermal reaction took place. After removal of excess of carbonyl, water and ether were added to the cooled mixture; then titration of the aqueous layer with silver nitrate revealed that 90% of the chlorine in the starting material had been liberated. The ethereal extract yielded 4-methylpenta-2 : 3-dienoic acid (3·8 g., 34%), m. p. 85—89°, and its ethyl ester (1·6 g., 11%).

2-Butylbuta-2 : 3-dienoic Acid.—In the same manner 1-chlorohept-2-yne [18] (10 g.) yielded 2-butylbuta-2 : 3-dienoic acid (4·05 g., 38%) as rhombs, m. p. 68—70° (Wotiz [9] gives m. p. 70°), and the corresponding ethyl ester (1·65 g., 13%), b. p. 86—90° (20 mm.), n_D^{18} 1·4581.

This reaction was examined under varied conditions, with results tabulated.

Buffer	Base (mole)	$Ni(CO)_4$	Time (hr.)	Temp.	Cl^- formed (mole)	Yield (%)
NaOAc–AcOH	1	0·25	0·5	40°	0·25	15
	1	1·0	0·5	40	0·96	43
	1	1·0	0·5	40	0·89	40
	1	1·0	16	20	0·45	23
	2	1·0	0·5	40	0·89	42
Na_2HPO_4–NaH_2PO_4 ...	1	1·0	0·5	40	—	9·5

The poor result with the phosphate buffer may be due to the poor solubility of these salts in the aqueous-alcoholic solvent.

Buta-2 : 3-dienoic Acid.—3-Chloroprop-1-yne [19] (6·7 g.), ethanol (30 c.c.), acetic acid (5·4 g.), sodium acetate (7·4 g.), and water (1·5 c.c.) were treated with nickel carbonyl (3·5 c.c.) at 60°. No exothermal reaction ensued. Isolation of the acid fraction gave an oil which failed to solidify and was sublimed at 50°/0·05 mm., yielding, after crystallisation from light petroleum (b. p. 40—60°), the acid (0·5 g., 6%) as plates, m. p. 60—62°, undepressed on admixture with an authentic sample prepared by the method of Eglinton *et al.*[10]

Hepta-2 : 3-dienoic Acid.—3-Chlorohex-1-yne [20] (11·7 g.), ethanol (30 c.c.), acetic acid (6 g.), sodium acetate (8·2 g.), and water (1·5 c.c.) were treated with nickel carbonyl (4 c.c.) in ethanol (5 c.c.). After isolation with ether, distillation yielded the *acid* (1·3 g., 10%), b. p. 86—90°/0·2 mm., n_D^{18} 1·4842 (Found: C, 66·8; H, 7·9. $C_7H_{10}O_2$ requires C, 66·6; H, 8·0%). It formed an amide (prepared *via* the acid chloride) which crystallised from benzene–light petroleum in rosettes of needles, m. p. 108—111°, and absorbed strongly at 1960 $cm.^{-1}$. Hydrogenation in ethyl acetate over platinum (uptake 97%) yielded *n*-heptanoic acid, identified by conversion into its amide, m. p. 95—96° (Robertson [21] gives m. p. 96°).

2-Butyl-4-methylpenta-2 : 3-dienoic Acid.—2-Chloro-2-methyloct-3-yne [22] (16 g.), ethanol (30 c.c.), acetic acid (6 g.), sodium acetate (8·2 g.), and water (1·5 c.c.) were treated with nickel carbonyl (4 c.c.). A mildly exothermal reaction occurred; isolation of the acid fraction followed by crystallisation from light petroleum (b. p. 40—60°) gave the acid as acicular prisms (2·15 g., 13%), m. p. 75—76° (Wotiz and Palchak [23] give m. p. 77—78°).

3-Chlorobut-1-yne (with J. M. Thompson).—A mixture of but-3-yn-2-ol (44 g.), pyridine (50 c.c.), and dry ether (60 c.c.) was added dropwise to a stirred solution of thionyl chloride (81 g.; freshly redistilled) in dry ether (60 c.c.) during 30 min. After 16 hours' stirring at 20°, water (200 c.c.) was added and the ethereal layer was separated and washed with sodium carbonate solution and water. Distillation of the dried ethereal solution through a 10 cm. Fenske column gave the *chloride* (23 g., 42%), b. p. 69°/758 mm., n_D^{18} 1·4256 (Found: C, 54·2; H, 6·0. C_4H_5Cl requires C, 54·25; H, 5·65%).

Penta-2 : 3-dienoic Acid.—3-Chlorobut-1-yne (8 g.) was added to a stirred and warmed

[18] Newman and Wotiz, *J. Amer. Chem. Soc.*, 1949, **71**, 1295.
[19] Hatch and Chiola, *ibid.*, 1951, **73**, 361.
[20] Hennion and Sheehan, *ibid.*, 1949, **71**, 1965.
[21] Robertson, *J.*, 1919, 1220.
[22] Campbell and Eby, *J. Amer. Chem. Soc.*, 1940, **62**, 1799.
[23] Wotiz and Palchak, *ibid.*, 1951, **73**, 1972.

mixture of ethanol (60 c.c.), sodium acetate (15·1 g.), acetic acid (10·8 g.), water (2·5 c.c.), and nickel carbonyl (14 c.c.). No exothermal reaction ensued, the temperature was kept at 40° for 30 min., and the mixture was worked up. A chloride estimation on the aqueous layer indicated 92% of the theoretical amount. On distillation the acid fraction, b. p. 51°/0·05 mm., rapidly solidified, and crystallisation from light petroleum (b. p. 40—60°) then gave the *acid* as needles (1·1 g., 12·5%), m. p. 38—40° (Found: C, 60·75; H, 6·2. $C_5H_6O_2$ requires C, 61·2; H, 6·15%).

4-Phenylbuta-2 : 3-dienoic Acid.—3-Chloro-3-phenylprop-1-yne [24] (15·1 g.) was added to a stirred mixture of ethanol (30 c.c.), acetic acid (6 g.), sodium acetate (8·2 g.), water (1·5 c.c.), and nickel carbonyl (4 c.c.) at 40°. A mildly exothermal reaction ensued and after removal of excess of nickel carbonyl by co-distillation the mixture was poured into water and extracted with ether. After extraction with sodium carbonate solution the aqueous layer was brought to pH 7 with hydrochloric acid, which liberated a polymeric mass. Removal of the latter by filtration was followed by acidification to pH 1 and ether-extraction. Evaporation of the dried extract and crystallisation of the residue from light petroleum (b. p. 40—60°)–ether gave the *acid* as rhombs (1·9 g., 12%), m. p. 94—96° (Found: C, 75·25; H, 5·3. $C_{10}H_8O_2$ requires C, 75·0; H, 5·05%).

Hydrogenation in ethyl acetate over platinum (uptake 95%) gave γ-phenylbutyric acid, m. p. 46—48° after two recrystallisations from water (Overbaugh, Allen, Martin, and Fieser [25] give m. p. 47—48°).

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[24] Levy and Cope, *J. Amer. Chem. Soc.*, 1944, **66**, 1687.
[25] Overbaugh, Allen, Martin, and Fieser, *Org. Synth.*, 1935, **15**, 64.

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931. *Researches on Acetylenic Compounds. Part LVIII.* The Structure of an Anomalous Reppe Carboxylation Product.*

By P. J. ASHWORTH, G. H. WHITHAM, and M. C. WHITING.

Interaction of nickel carbonyl and 1-bromo- or 1-iodo-hept-2-yne yields the *cyclo*pentenone derivative (I). Its structure, deduced from degradative and spectroscopic evidence, was proved by the rational synthesis of the dihydro-derivative (V) of its lower homologue.

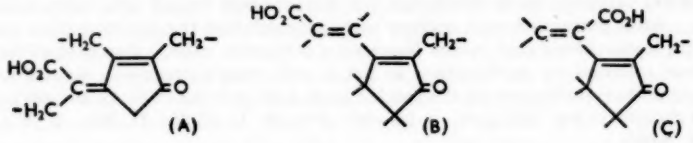
AFTER the investigations described in the preceding paper, the action of nickel carbonyl on 1-bromohept-2-yne was examined, the reaction conditions being those employed for the corresponding chloride. Again the main product was 2-butylbuta-2 : 3-dienoic acid, but a second acid, m. p. 106—107°, was also formed, and was separated by fractional crystallisation. A much smaller quantity of the new acid was formed, along with the allenic acid, when the corresponding toluene-*p*-sulphonate was used, while the iodide gave it as the main product.

The new acid possessed the empirical formula $C_{16}H_{24}O_3$ and (from the volatility of its ester) was clearly monomeric. It showed an absorption maximum at 2940 Å (ε 15,000). Infrared bands at 1709, 1665, and 1635 cm.$^{-1}$ could not be usefully interpreted and attempts were therefore made to prepare a methyl ester. This ester was not formed at an appreciable rate in methanolic sulphuric acid, but was obtained with diazomethane. It showed an ultraviolet absorption spectrum similar to that of the acid, and infrared bands at 1730 and 1706 cm.$^{-1}$. The former was clearly the carbonyl stretching frequency of an ester group, and the latter that of a ketonic function. The ester in fact formed a 2 : 4-dinitrophenylhydrazone, which had $\lambda_{max.}$ 3970 Å in ethanol, and was therefore doubly conjugated; [1] if, however, the ketone group is conjugated, then its infrared stretching frequency indicates that it must be present in a five-membered ring.

* Part LVII, preceding paper.

[1] Braude and E. R. H. Jones, *J.*, 1945, 498.

Further progress was made by catalytic hydrogenation. With platinic oxide in ethyl acetate, the new acid absorbed one mol., giving a crystalline acid $C_{16}H_{26}O_3$ with $\lambda_{max.}$ 2380 Å. Its methyl ester showed strong infrared bands at 1740 and 1706 cm.$^{-1}$, indicating that the ketonic function was still conjugated but the ester group no longer so. The 2 : 4-dinitrophenylhydrazone had $\lambda_{max.}$ 3870 Å, indicating one conjugated ethylenic linkage.[1] Further, if the dihydro-acid was a *cyclo*pentenone, it must be αβ-disubstituted, since 2- and 3-monosubstituted (monomethyl)*cyclo*pentenones[2,3] absorb maximally at only 2290 and 2250 Å, respectively; 2 : 3-dimethyl*cyclo*pentenone[2] has $\lambda_{max.}$ 2370 Å.



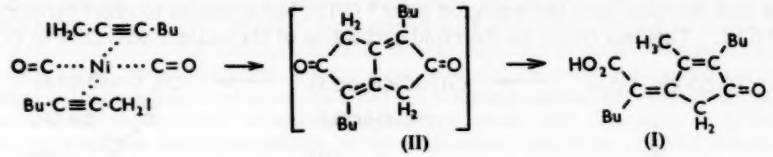
There are thus only three possible partial formulæ (A–C), if these spectroscopic results are to be fully explained, and of these structures, (C), a vinylogous β-keto-acid, would require that the acid $C_{16}H_{24}O_3$ or at least its dihydro-derivative should be readily decarboxylated. In fact, both these acids were stable to high temperatures and to hydrolytic conditions. Formula B cannot be expanded to any structure even remotely related to that of the starting material. On the other hand, (A) can be expanded to (I), which might be formed from a symmetrical precursor (II) obtained from two molecules of iodoheptyne and two carbon monoxide residues. The diketone (II) might well be sufficiently unstable, through strain and through the unfavourable orientation of the two polar carbonyl groups, to undergo a reversed Claisen condensation in the presence of water alone, or helped by the nickel salts present (weak Lewis acids), giving the acid (I). This is not a necessary assumption, as the four groupings might instead be held in a nickel complex until the attack of a water molecule resulted in direct transformation to the acid (I).

Ozonolysis of the new acid gave no volatile carbonyl compounds, and no keto-fraction could be isolated. Valeric acid (0·6 mol.) was obtained, along with non-crystallisable material. Vigorous hydrogenation resulted in an uptake of exactly 3 mols., giving a non-ketonic product transparent in the ultraviolet region down to 2000 Å (hence, directly, the acid must be monocyclic), which was partly dehydrated to a lactone on distillation. Assuming *cis*-addition, one would expect to obtain four stereoisomeric hexahydro-derivatives from the acid (I), two of which could lactonise; the carbonyl stretching frequency, 1770 cm.$^{-1}$, observed for the lactone produced is intermediate between those[4] of normal γ-(*ca.* 1780 cm.$^{-1}$) and δ-lactones (*ca.* 1740 cm.$^{-1}$), and therefore not implausible for a strained δ-lactone such as (III). For somewhat similar lactones, Wilder and Winston[5] found a band at 1760 cm.$^{-1}$. The Zimmerman test for $-CH_2{\cdot}CO-$ in the acid (I) was positive. Although no crystalline product could be obtained, the crude product of reduction of the methyl ester by lithium aluminium hydride showed $\lambda_{max.}$ 2410 Å, in good agreement with 2450 Å calculated[6] for the glycol (IV). All these results are consistent with the structure (I), as is the failure to effect acid-catalysed esterification, since a model reveals steric hindrance in the corresponding transition state—this is the only evidence for the configuration about the exocyclic linkage assumed here.

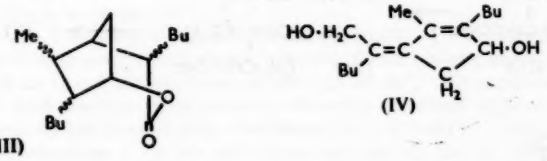
Several attempts were made to complete the degradation of the acid (I) by a further reversed Claisen condensation, which should give αα′-dibutyl-ββ′-dimethylmuconic acid or one of its derivatives. All were unsuccessful, the ester surviving, *e.g.*, after three hours in boiling 10% sodium methoxide solution. A rational synthesis of a compound related

[2] Hennion and Davis, *J. Org. Chem.*, 1951, **16**, 1289.
[3] Acheson and Robinson, *J.*, 1952, 1131.
[4] R. N. Jones, Humphries, and Dobriner, *J. Amer. Chem. Soc.*, 1950, **72**, 956.
[5] Wilder and Winston, *ibid.*, 1955, **77**, 5598.
[6] Woodward, *ibid.*, 1942, **64**, 72.

to (I) was therefore considered necessary, and the choice fell upon the dihydro-derivative (V) of the analogous acid (VI) in which methyl groups replace the *n*-butyl groups.

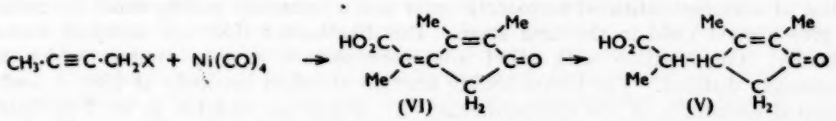


(II) (I)



(III) (IV)

It proved necessary first to find a more convenient route to but-2-yn-1-ol than published procedures. 2 : 3-Dichlorobutan-1-ol was prepared, but gave a poor yield on dehydrochlorination; 3-chlorobut-2-en-1-ol, however, was dehydrochlorinated by sodamide in liquid ammonia in much better yield than by potassium hydroxide.[7] Conversion into the acetylenic chloride and metathesis with sodium iodide proceeded normally, but



(VI) (V)

1-iodobut-2-yne gave only a minute yield of the expected keto-acid (VI) on treatment with nickel carbonyl, the main product being dimethylmaleic anhydride. This implies a new variant of the Reppe carboxylation, in which the acetylene and carbon monoxide are involved in the ratio 1 : 2, not hitherto observed. It has not been investigated further, except that the order of addition of the reactants was shown not to affect the result.

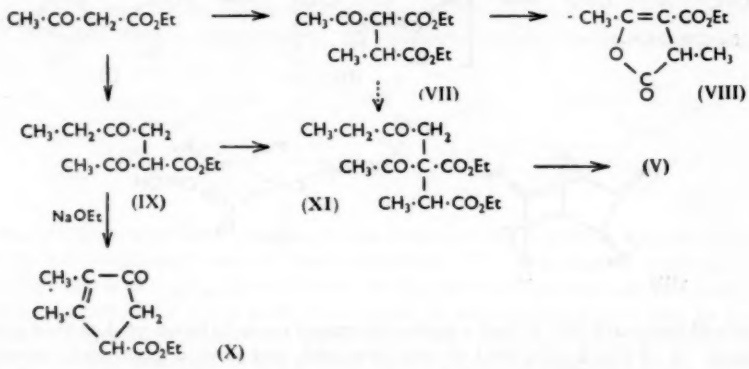
When 1-bromobut-2-yne was employed, the yield of acid (VI) was comparable with that obtained from 1-bromohept-2-yne, although the other product was again dimethylmaleic anhydride, rather than the allenic acid. When the chloride was employed, a small yield of the acid (VI) was obtained—whereas 1-chlorohept-2-yne gave no trace of acid (I), according to spectroscopic measurements—and the expected 2-methylbuta-2 : 3-dienoic acid was obtained in quantity. Dimethylmaleic anhydride was not formed in this reaction, and hence cannot be a normal product from the allenic acid and nickel carbonyl. The reasons for the different behaviour of the two homologous sets of halides are not obvious, but *n*-butylmethylmaleic anhydride might well have been formed in small yield from the iodoheptyne, and yet escaped detection.

Hydrogenation of acid (VI) readily gave acid (V) under conditions similar to those used for the higher homologue. The analogy between the two series was proved by abundant spectroscopic data, and further evidence for the structures (I) and (VI) was made available by pK_a measurements on the more soluble lower homologues; values of 3·1 and 4·4 for acids (VI) and (V), respectively, testify to the C=O grouping cross-conjugated to the carboxyl residue in acid (VI), and the interruption of the conjugation, and hence of the transfer of polarisation, in acid (V).

[7] Hatch and Nesbit, *J. Amer. Chem. Soc.*, 1950, **72**, 727.

The synthesis envisaged for the dihydro-derivative (V) was based upon the work of Willstätter and Clark,[8] and involved condensation of ethyl acetoacetate successively with ethyl α-bromopropionate and 1-chlorobutan-2-one, as shown.

The first reaction gave the expected ester [9] (VII), but attempts to effect further alkylation failed. This was traced to the rapid cyclisation of the sodium derivative of (VII) to



the enol-lactone (VIII), recognised by its absorption band at 1810 cm.$^{-1}$; an analogous reaction has been observed previously.[10]

The order of alkylation was therefore inverted, although it was realised that the interaction of a monosubstituted acetoacetic ester and a secondary halide would be unlikely to give a good yield in the final stage. The diketo-ester (IX) was obtained without difficulty. Condensation with ethyl α-bromopropionate gave a product which was fractionally distilled. The lowest-boiling fraction absorbed intensely at 2380 Å and so consisted essentially of the *cyclo*pentenone (X), which was isolated as its 2 : 4-dinitrophenylhydrazone. This cyclisation of ester (IX) took place under the action of ethoxide alone. The second fraction consisted mainly of the unchanged diketo-ester (IX); the highest-boiling fraction also absorbed intensely at ~2380 Å, and was probably a mixture of the desired ester (XI) and its cyclisation product. Alkaline hydrolysis gave a syrupy acidic fraction which was subjected to paper chromatography; a spot, developed either by 2 : 4-dinitrophenylhydrazine or by a pH indicator, was found with an R_F value corresponding to that of acid (V). After fractional precipitation, a crystalline specimen of the latter, identical with the product obtained by the hydrogenation of acid (VI), was obtained in small yield. It is not known in which order the condensation, cyclisation, decarbethoxylation, and (possibly) epimerisation steps had occurred, but the formation of acid (V) from ethyl α-bromopropionate and ester (IX) provides the necessary confirmation of the structures assigned to the anomalous Reppe carboxylation products.

Experimental

Reaction between 1-Bromohept-2-yne and Nickel Carbonyl.—1-Bromohept-2-yne [11] (6·7 g.) was added to a stirred mixture of ethanol (30 c.c.), acetic acid (4·6 c.c.), sodium acetate (6·4 g.), water (1·5 c.c.), and nickel carbonyl (6 c.c.) at 45° during 20 min. No exothermal reaction ensued. The mixture was worked up and the acid fraction was isolated as a crystalline solid. Repeated recrystallisation from light petroleum (b. p. 60—80°) gave *2-butyl-4-1'-carboxypentylidene-3-methylcyclopent-2-enone* (I) as plates (0·5 g., 10%), m. p. 103—105°, raised to 106—107° on recrystallisation from aqueous ethanol (Found: C, 72·55; H, 9·5%; equiv., 259. $C_{16}H_{24}O_3$

[8] Willstätter and Clark, *Ber.*, 1914, **47**, 291.
[9] Conrad, *Annalen*, 1877, **188**, 226.
[10] Sprankling, *J.*, 1897, **71**, 1163.
[11] Newman and Wotiz, *J. Amer. Chem. Soc.*, 1949, **71**, 1295.

requires C, 72·7; H, 9·15%; equiv., 264). Evaporation of the mother-liquors from the initial crystallisation followed by recrystallisation of the residue from light petroleum (b. p. 40—60°) gave 2-butylbuta-2 : 3-dienoic acid (0·6 g., 11·5%), m. p. 68°.

Reaction between Hept-2-yn-1-yl Toluene-p-sulphonate and Nickel Carbonyl.—Hept-2-yn-1-yl toluene-*p*-sulphonate (5 g.; prepared from hept-2-yn-1-ol by the method of Eglinton and Whiting [12]) in ethanol (5 c.c.) was added during 30 min. to a stirred mixture of ethanol (30 c.c.), acetic acid (4·6 c.c.), sodium acetate (6·4 g.), water (1·5 c.c.), and nickel carbonyl (6 c.c.) at 40°. The solution became green and crystalline sodium toluene-*p*-sulphonate appeared. Working up gave a solid acid fraction; trituration of this with warm light petroleum (b. p. 40—60°) followed by filtration and crystallisation of the undissolved solid from aqueous ethanol gave the acid (I) (0·05 g., 2%), m. p. 103—105°. Evaporation of the filtrate and crystallisation of the residue from light petroleum (b. p. 40—60°) yielded 2-butylbuta-2 : 3-dienoic acid as prisms (0·81 g., 31%), m. p. 68—70°.

Reaction between 1-Iodohept-2-yne and Nickel Carbonyl.—1-Iodohept-2-yne (33·1 g.) [13] was added during 30 min. to a stirred mixture of ethanol (90 c.c.), acetic acid (18 g.), sodium acetate (24 g.), water (5 c.c.), and nickel carbonyl (20 c.c.) at 40°. No exothermal reaction ensued. Isolation of the acid fraction, after removal of excess of nickel carbonyl, gave an oil which partly crystallised on addition of light petroleum (b. p. 40—60°). Filtration and recrystallisation from light petroleum (b. p. 60—80°) gave the acid (I) (2·8 g., 14·5%), m. p. 102—105°. Evaporation of the mother-liquors followed by recrystallisation from light petroleum (b. p. 40—60°) afforded 2-butylbuta-2 : 3-dienoic acid, m. p. 66—68° (0·97 g., 5%). Distillation of the neutral fraction gave ethyl 2-butylbuta-2 : 3-dienoate (4·6 g., 17%), b. p. 89°/14 mm., n_D^{17} 1·4589.

Methyl Ester of the Acid (I).—The acid (1 g.) in ether (10 c.c.) was treated with ethereal diazomethane until evolution of nitrogen ceased and a yellow colour persisted. After being washed with sodium carbonate solution to remove unchanged acid (120 mg. recovered) the solution was dried and distilled, yielding the *methyl ester* (0·72 g., 78%), b. p. 180° (bath)/0·01 mm., n_D^{18} 1·5152 (Found: C, 72·55; H, 9·05. $C_{17}H_{26}O_3$ requires C, 73·35; H, 9·4%). The 2 : 4-*dinitrophenylhydrazone* crystallised in bright red needles from ethyl acetate–ethanol and had m. p. 136—137° (Found: C, 60·3; H, 6·35; N, 12·4. $C_{23}H_{30}O_6N_4$ requires C, 60·25; H, 6·6; N, 12·2%).

Hydrogenation of Acid (I).—The acid (364 mg.) was hydrogenated in "AnalaR" ethyl acetate (25 c.c.) with platinic oxide (100 mg.) (uptake 0·95 mol.). After filtration, evaporation, and crystallisation from light petroleum (b. p. 40—60°) 2-*butyl*-4-1′-*carboxypentyl*-3-*methylcyclopent*-2-*enone* was obtained as prisms (270 mg., 74%), m. p. 83—85° (Found: C, 72·5; H, 9·7. $C_{16}H_{26}O_3$ requires C, 72·2; H, 9·85%). This dihydro-acid (390 mg.) with diazomethane gave a *methyl ester* (290 mg., 71%, b. p. 180° (bath)/0·1 mm., n_D^{18} 1·4787 (Found: C, 73·0; H, 10·0. $C_{17}H_{28}O_3$ requires C, 72·8; H, 10·05%), whose 2 : 4-*dinitrophenylhydrazone* crystallised as red needles (from ethyl acetate–ethanol), m. p. 115—116° (Found: C, 60·0; H, 7·3, N, 12·3. $C_{23}H_{32}O_6N_4$ requires C, 60·0; H, 7·00; N, 12·15%),

Zinc Dust–Acetic Acid Reduction of the Acid (I).—A solution of the acid (500 mg.) in acetic acid (20 c.c.) was heated under reflux and zinc dust (5 g.) was added in portions during 1 hr. After cooling, water was added and the solution was extracted with ether. Evaporation of the dried extract gave an oil which slowly solidified and crystallised from light petroleum (b. p. 40—60°) to give the dihydro-acid (290 mg., 58%), m. p. and mixed m. p. 85—86°.

Complete Hydrogenation of Acid (I).—The acid (337 mg.) was hydrogenated in acetic acid (20 c.c.) over platinic oxide (200 mg.) (uptake 2·94 mols.). Filtration, evaporation, and distillation gave a liquid, b. p. 180° (bath)/0·01 mm., n_D^{18} 1·4665 (Found: C, 74·55; H, 11·2. Calc. for $C_{16}H_{30}O_3$: C, 71·05; H, 11·2%. Calc. for $C_{16}H_{28}O_2$: C, 76·15; H, 11·2%), evidently a mixture of hydroxy-acid and lactone.

Ozonolysis of the Acid (I).—A slow stream of ozonised oxygen was passed through a solution of the acid (516 mg.) in ethyl acetate (20 c.c.) for 2 hr. at 18°. After evaporation of the solvent and decomposition of the ozonide by zinc dust (2 g.) and warm water, the neutral and the acid fraction were isolated with ether. Evaporation of the former left a negligible residue which did not react with 2 : 4-dinitrophenylhydrazine reagent, while the latter yielded *n*-valeric acid (120 mg.), identified as the amide, m. p. (after three recrystallisations from benzene) and mixed m. p. 104—105°

[12] Eglinton and Whiting, *J.*, 1950, 3650.
[13] Toussaint and Wenzke, *J. Amer. Chem. Soc.*, 1935, **57**, 669.

2 : 3-*Dichlorobutan*-1-*ol*.—Chlorine (114 g.) in carbon tetrachloride (100 c.c.) was added to a stirred and cooled solution of but-2-en-1-ol (114 g.), at −40° to −50°. The mixture was allowed to warm to room temperature and the solvent was evaporated. Distillation of the residual oil gave **2 : 3-*dichlorobutan*-1-*ol*** (94 g., 41%), b. p. 62°/5 mm. n_D^{19} 1·4783 (Found: C, 33·55; H, 5·70. $C_4H_8OCl_2$ requires C, 33·60; H, 5·65%). A considerable quantity of heterogeneous high-boiling material remained.

But-2-*yn*-1-*ol*.—(a) *From* **2 : 3-*dichlorobutan*-1-*ol***. 2 : 3-Dichlorobutan-1-ol (94 g.) was added dropwise to a solution of sodamide (from sodium, 55 g.) in liquid ammonia (800 c.c.) during 2 hr. After 12 hours' stirring the complex was decomposed with ammonium chloride (128 g.), ether (600 c.c.) was added, and the mixture was set aside until the ammonia had evaporated. Evaporation of the dried ethereal solution followed by distillation gave but-2-yn-1-ol (23 g., 49%), b. p. 45°/16 mm., n_D^{20} 1·4542.

(b) *From* 3-*chlorobut*-2-*en*-1-*ol*. 3-Chlorobut-2-en-1-ol (134 g.) was added during 30 min. to a suspension of sodamide (from sodium, 65 g.) in liquid ammonia (3 l.). The mixture was stirred overnight, then ammonium chloride (148 g.) was added in portions at a rate that permitted control of the reaction. The ammonia was allowed to evaporate and the residue was extracted thoroughly with ether (5 × 250 c.c.). The ether was removed through a 20 cm. Fenske column; distillation of the residue yielded 66—75 g. (75—85%) of but-2-yn-1-ol, b. p. 55°/18 mm., n_D^{20} 1·4550.

1-*Iodobut*-2-*yne*.—1-Chlorobut-2-yne [14] (5·3 g.) was stirred and heated under reflux with sodium iodide (10 g.) in acetone (100 c.c.) for 15 hr. After filtration of the sodium chloride and washing with ether the filtrate was distilled to a small bulk to remove most of the acetone. The sodium chloride was dissolved in water; ether-extracts of the solution together with the residue from the above distillation were washed with sodium thiosulphate solution, dried, and evaporated through a short Fenske column. Distillation of the residue gave the iodide (6·7 g., 63%), b. p. 51—52°/16 mm., n_D^{18} 1·5859, with the expected very simple infrared spectrum.

1-*Bromobut*-2-*yne*.—But-2-yn-1-ol (100 g.) in dry ether (80 c.c.) and pyridine (1 c.c.) were treated with phosphorus tribromide (140 g.) in ether (53 c.c.) at such a rate as to maintain gentle boiling. After being heated under reflux for a further 2 hr. the solution was cooled and the colourless ether layer was removed and washed with potassium hydrogen carbonate solution (50 c.c.), then water (50 c.c.). Evaporation of the ether and distillation gave the *bromide* (105 g., 55%), b. p. 82°/136 mm., n_D^{21} 1·5113 (Found: C, 36·4; H, 4·0. C_4H_5Br requires C, 36·1; H, 3·8%).

Reaction between 1-*Iodobut*-2-*yne and Nickel Carbonyl*.—1-Iodobut-2-yne (10 g.) was added to a stirred mixture of ethanol (23·5 c.c.), acetic acid (4·8 g.), sodium acetate (6·4 g.), water (1 c.c.), and nickel carbonyl (6·4 c.c.) at 45° during 20 min. No exothermal reaction ensued so the reaction mixture was kept at 40° for a further 30 min. After cooling and removal of excess nickel carbonyl by co-distillation with ether (100 c.c.), the residue was treated with 5% sulphuric acid (100 c.c.), extracted with ether, and separated into acid and neutral fractions. The acid fraction was isolated as brown crystals. **4-1′-*Carboxyethylidene*-2 : 3-*dimethyl*cyclo-*pent*-2-*enone*** (VI) which remained after extraction with light petroleum (b. p. 40—60°) recrystallised from ether (100 mg., 1%) and had m. p. 199° (Found: C, 66·35; H, 6·65. $C_{10}H_{12}O_3$ requires C, 66·65; H, 6·7%). Light absorption: max. at 2040 and 2940 Å (ε 8000 and 15,000 respectively). Evaporation of the light petroleum extracts followed by recrystallisation from light petroleum (b. p. 40—60°) gave dimethylmaleic anhydride as plates (1 g., 14%), m. p. 94·5° (Found: C, 57·15; H, 4·8. Calc. for $C_6H_6O_3$: C, 57·15; H, 4·75%).

Reaction between 1-*Bromobut*-2-*yne and Nickel Carbonyl*.—Nickel carbonyl (38·5 c.c.) was added to a stirred mixture of 1-bromobut-2-yne (50 g.), ethanol (85 c.c.), acetic acid (33 g.), sodium acetate (40·7 g.), and water (3 c.c.) at 45°. No exothermal reaction ensued, but on working up a solid acid fraction was obtained. Trituration with warm light petroleum (b. p. 40—60°) followed by filtration and crystallisation of the undissolved solid from ether gave the acid (VI) (1·2 g., 5%), m. p. 199°. Evaporation of the filtrate and recrystallisation of the residue from light petroleum (b. p. 40—60°) yielded dimethylmaleic anhydride (1·3 g., 3%), m. p. 94·5°.

Reaction between 1-*Chlorobut*-2-*yne and Nickel Carbonyl*.—Nickel carbonyl (19 c.c.) was added to a stirred mixture of 1-chlorobut-2-yne (30 g.), ethanol (70 c.c.), acetic acid (21 g.), sodium acetate (28 g.), and water (3 c.c.) at 45°. No exothermal reaction ensued. Isolation

[14] Hatch and Chiola, *J. Amer. Chem. Soc.*, 1951, **73**, 360.

of the acid fraction, after removal of the excess of nickel carbonyl in the usual way, gave a light brown solid. Extraction with light petroleum (b. p. 40—60°) and crystallisation of the undissolved solid from ether gave the acid (VI) (300 mg., 2%), m. p. 199°. Evaporation of the mother-liquors followed by recrystallisation of the residue from light petroleum (b. p. 40—60°) afforded **2-*methylbuta*-2 : 3-*dienoic*** acid as needles (5 g., 15%), m. p. 70° (Found: C, 61·15; H, 6·05. $C_5H_6O_2$ requires C, 61·2; H, 6·1%).

Hydrogenation of Acid (VI).—The acid (500 mg.) was hydrogenated in ethyl acetate with platinic oxide (uptake 1 mol.). After filtration, evaporation, and crystallisation from benzene containing 10% of light petroleum (b. p. 60—80°), **4-1′-*carboxyethyl*-2 : 3-*dimethyl*cyclo*pent*-2-*enone*** (V) was obtained (350 mg., 70%), having m. p. 123—124° (Found: C, 66·15; H, 7·75. $C_{10}H_{14}O_3$ requires C, 65·95; H, 7·75%). Light absorption: max. at 2360 Å (ε 14,000).

Methyl Ester of Acid (V).—Treatment with standardised ethereal diazomethane (1 mol.) and crystallisation from methanol gave the ***methyl ester*** (65%), m. p. 78° (Found: C, 67·95; H, 7·15. $C_{11}H_{16}O_3$ requires C, 67·3; H, 8·2%).

Determination of the Dissociation Constants.—The acids were dissolved in distilled water and their pK values were determined by potentiometric titration with carbonate-free 0·01N-sodium hydroxide, a glass electrode and a Cambridge pH meter at 25° being used.

Ethyl* 4-*Oxopentane*-2 : 3-*dicarboxylate (VII).—Sodium (9 g.) was added to ethyl acetoacetate (42 g.) in dry ethanol (100 c.c.). When reaction had ceased, ethyl α-bromopropionate (63 g.) was added and the mixture was heated under reflux for 12 hr., cooled, poured into water, and extracted with ether. Evaporation, and distillation of the residue, yielding the ester (38 g.), b. p. 83·5°/0·05 mm., n_D^{20} 1·4340 (Found: C, 57·20; H, 7·65. Calc. for $C_{11}H_{16}O_5$: C, 57·40; H, 7·80%).

1-*Chlorobutan*-2-*one*.—Potassium hydroxide (72 g.) was dissolved in hot propan-1-ol (275 c.c.) in a 3-l. three-necked flask. Two dropping funnels and a Fenske column were fitted and the column was connected through a condenser and adaptor to a 3-l. filter-flask fitted with a calcium chloride drying tube and cooled in ice. The contents of the flask were cooled and dry ether (600 c.c.) was added. Methyl *N*-nitrosourethane (120 c.c.) and dry ether were slowly added from the two funnels, and when the flask was warmed ether and diazomethane co-distilled, the quantity of ether in the flask being kept constant. When the condensed liquid became colourless, the distillate was transferred to a 3-l. three-necked flask equipped with mechanical stirrer, dropping funnel, and condenser. Propionyl chloride (27·6 g.) in dry ether (50 c.c.) was slowly added, nitrogen being evolved. After 2 hr., the diazo-ketone solution was cooled in ice-water and treated with dry hydrogen chloride until effervescence ceased. Water (400 c.c.) was added and the ethereal layer was separated, washed with potassium hydrogen carbonate solution, and dried ($MgSO_4$). The ether was removed through a short Fenske column, and the residue on distillation gave 1-chlorobutan-2-one (25 g., 81%), b. p. 65°/50 mm., n_D^{20} 1·4352.

Ethyl* 2 : 5-*Dioxoheptane*-3-*carboxylate (IX).—Dry ether (100 c.c.) was added to sodium (6·8 g., powdered under boiling xylene). Ethyl acetoacetate (39 g.), diluted with dry ether (50 c.c.), was slowly added while the ether refluxed. The sodio-derivative, after being kept overnight at room temperature, was cooled in a salt–ice bath and 1-chlorobutan-2-one (28·6 g.) in dry ether (50 c.c.) was slowly added. The mixture was stirred for 20 hr. at room temperature and 2 hr. on the steam-bath. The precipitated sodium chloride was dissolved in water (100 c.c.). Isolation of the keto-ester followed by distillation yielded ***ethyl* 2 : 5-*dioxoheptane*-3-*carboxylate*** (27 g., 54%), b. p. 85°/0·01 mm., n_D^{25} 1·4430 (Found: C, 59·7; H, 7·9. $C_{10}H_{16}O_4$ requires C, 60·0; H, 8·0%).

***Reaction between Ethyl* 2 : 5-*Dioxoheptane*-3-*carboxylate* and *Ethyl* α-*Bromopropionate*.**—Sodium (2·4 g.) was added to the diketo-ester (17 g.) in dry ethanol (50 c.c.). When the reaction had ceased, ethyl α-bromopropionate (18·5 g.) was added, and the mixture was heated under reflux for 4 hr. Isolation of the neutral fraction with ether and distillation gave three groups of fractions:

(*a*) B. p. *ca.* 65°/0·01 mm., n_D^{17} 1·4659 (3·2 g.). This had $\lambda_{max.}$ 2350 Å (ε 9000) and gave the **2 : 4-*dinitrophenylhydrazone***, m. p. 142°, $\lambda_{max.}$ 3870 Å (ε 31,000), of ethyl 2 : 3-dimethyl-4-oxo-*cyclo*pent-2-enecarboxylate (Found: C, 52·75; H, 5·1; N, 15·05. $C_{16}H_{18}O_6N_4$ requires C, 53·0; H, 5·0; N, 15·45%).

(*b*) B. p. *ca.* 95°/0·1 mm., n_D^{17} 1·4575 (3·0 g.), which appeared to be a mixture of the foregoing *cyclo*pentenone with a larger proportion of starting material and had $\lambda_{max.}$ 2380 Å (ε 4100).

(*c*) B. p. 120° (bath temp.)/10^{-4} mm., n_D^{17} 1·4720 (2·8 g.), which had $\lambda_{max.}$ 2390 Å (ε 9000) and

appeared to be essentially the desired condensation and cyclisation product, probably with partial loss of the tertiary ethoxycarbonyl grouping.

Fraction (*c*) (1·3 g.) was treated with 10% methanolic sodium hydroxide, giving a syrupy acid (730 mg.) which was dissolved in benzene (25 c.c.). Addition of light petroleum (5 c.c.) precipitated brown polymeric matter which was removed. Further addition of light petroleum precipitated a solid which was recrystallised from benzene–light petroleum, giving the acid (V) (113 mg.), m. p. 124°, undepressed on admixture with a specimen prepared as above.

We thank Mr. E. S. Morton and his assistants for microanalyses, and Miss W. Peadon and Mrs. J. Shallcross for ultraviolet and infrared spectroscopic determinations, the latter carried out under the supervision of Dr. G. D. Meakins. We are indebted to the Department of Scientific and Industrial Research for a Maintenance Grant to one of us (G. H. W.). The nickel carbonyl used was kindly provided by the Mond Nickel Company Ltd.

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932. *Physicochemical Studies on Starches. Part VIII.* Further Observations on the Fractionation of Potato Starch.*

By J. M. G. COWIE and C. T. GREENWOOD.

The fractionation conditions necessary to achieve effective separation and minimise degradation of the components of potato starch have been critically examined. Laboratory-prepared and *commercial* starch samples have been compared. The amylose from commercial starch is much smaller ($\overline{D.P.}$ ~2500 glucose residues) than that from the laboratory-prepared sample ($\overline{D.P.}$ ~4000), and the effect of aqueous leaching at 70° and 98° also differs. The uniformity of structure of amylose in the granule is discussed. " Sub-fractions " obtained during the recrystallisation of the fractionation products of the laboratory-prepared starch have also been studied.

IN Part VI of this Series,[1] we reported the results of aqueous leaching at various temperatures on laboratory-prepared potato-starch granules. The problem of fractionation and the fine structure of the starch granule are further considered here. It is essential to obtain the separated components in an unmodified form, and artefacts or degradation products must be avoided. Amylose is susceptible to oxidative degradation at elevated temperatures.[2] The extent to which this occurs during fractionation has now been examined in detail, as have methods suggested[3] for minimising this effect. Commercial potato starch has also been fractionated. In addition, the " sub-fractions " obtained during recrystallisation of the amylose component of laboratory-prepared starch have been studied in an attempt to establish the presence of material intermediate in structure between amylose and amylopectin.

EXPERIMENTAL

Preparation of Starch.—Starch was extracted from potatoes (var. Golden Wonder) by the method outlined previously.[4] A sample of commercial potato starch (" Superfine Farina ") was kindly supplied by Messrs. Brown & Polson, Ltd.

Fractionation Methods.—The methods of fractionation were as shown in Table 1.

Characterisation of Fractionation Products.—Measurements of (*a*) iodine affinity (I.A.),[5] (*b*) limiting viscosity number $[\eta]$ in M-potassium hydroxide,[4] and (*c*) sedimentation velocity in

* Part VII, *J. Polymer Sci.*, 1957, in the press.

[1] Cowie and Greenwood, *J.*, 1957, 2862.
[2] Bottle, Gilbert, Greenwood, and Saad, *Chem. and Ind.*, 1953, 541.
[3] Greenwood, *Adv. Carbohydrate Chem.*, 1956, **11**, 335.
[4] Cowie and Greenwood, *J.*, 1957, 2658.
[5] Anderson and Greenwood, *J.*, 1955, 3016.

0·2M-potassium hydroxide [6] were carried out on the separated components as detailed previously.

Results and Discussion

Our previous results [1] have shown that amylose isolated from laboratory-prepared potato starch possesses a number-average degree of polymerisation ($\overline{D.P.}$) of the order of 4000 glucose units. This value was therefore taken as a standard to judge the effect of modifications in fractionation techniques.

Oxidative Degradation.—Many investigators have suggested that starch, particularly the linear amylose component, may be degraded during fractionation procedures.[3] By measuring the molecular weight of the separated components, we have shown that the presence of oxygen during fractionation is, in fact, a serious source of degradation. The results in Table 1 (cf. F1 and F2) show that the $\overline{D.P.}$ of the amylose produced by passage

Table 1. *Fractionation methods and the properties of the separated components.*

Expt.	Fractionation method: Precipitant	Atm.	Ref.	Component	[η]	I.A. (%)	Purity [a] (%)	$\overline{D.P.}$ [b]
F 1	Thymol, then Bu^{n}OH	N_2	1	Initial-complex	—	14·2	74	—
				Amylose †	500	19·5	100	3700
				Amylose ‡	440	19·5	100	3200
				Amylopectin	180	0·16	99·2	—
F 2	Thymol, then Bu^{n}OH	O_2	1	Amylose §	272	—	—	2000
				Amylose ‖	220	—	—	1600
				Amylopectin	138	—	—	—
F 3	Thymol, then Bu^{n}OH	Air	1	Amylose	350	—	—	2600
				Amylopectin	176	—	—	—
F 4 *	Thymol, then Bu^{n}OH	N_2	1	Initial-complex	—	15·5	79·5	—
				Amylose	340	—	—	2500
				Amylopectin	170	0·3	98·5	
F 5 *	Aq. leaching at 70°	N_2	1	Amylose	330	—	—	2400
				Amylopectin	—	2·3	88·2	—
F 6 *	Fractionation after leaching at 70°	N_2	1	Amylose	330	—	—	2400
				Amylopectin	170	—	—	—
F 7	Aq. leaching at 70°	N_2	1	Amylose	240	19·5	100	1800
				Amylopectin	—	2·5	88	—
F 8	Fractionation after leaching at 70°	N_2	1	Amylose	560	19·5	100	5300
				Amylopectin	—	0·04	99·8	—
F 9	Pyridine	N_2	8	Initial complex	—	17·2	90·5	—
				Amylose	360	—	—	2700
				Amylopectin	165	0·7	96·4	—
F 10	Pentanol	N_2	9	Initial complex	—	14·0	72·0	—
				Amylose	405	—	—	3000
				Amylopectin	180	0·1	99·5	—
F 11	KOH-dispersion, then pentanol	N_2	10	Amylose	395	—	—	2900
				Amylopectin	180	—	—	—
F 12	Thymol and BuOH + *N*-phenyl-2-naphthylamine	Air	3	Amylose	330	—	—	2400
F 13	Thymol and BuOH + quinol	Air	3	Amylose	100	—	—	740

[a] Purity calc. as in Table of ref. 1. [b] D.P. calc.[1] from $\overline{D.P.} = 7{\cdot}4[\eta]$ for amylose.
* Fractionation using commercial starch. † Small-scale (500 ml.) fractionation. ‡ Large-scale (3 l.) fractionation. § Recrystalln. under N_2. ‖ Recrystalln. under O_2.

of oxygen through the fractionation and recrystallisation media is reduced by one half (equivalent to *ca.* 1·2 bonds broken/initial amylose molecule). Even when the recrystallisations are carried out under nitrogen, degradation is still appreciable. Amylopectin is also depolymerised under these exaggerated conditions.

Fractionation in the presence of air (F3) results in a less drastic but still appreciable decrease in $\overline{D.P.}$; the amylose undergoes the scission of 0·2—0·5 bond/molecule, whilst viscometrically the amylopectin is virtually unchanged.

Oxidative degradation can also occur during isolation of the amylose complex. A

[6] Bryce, Cowie, and Greenwood, *J. Polymer Sci.*, 1957, **25**, 251.

Sharples supercentrifuge was used originally.[7] It has since been shown that oxygen-free conditions cannot be maintained during centrifugation, and excessive use of this instrument causes some degradation. (For example, after ½, 1, and 1½ hours' centrifugation, the limiting viscosity number of a given amylose sample was 400, 365, and 375.) The Sharples centrifuge is now only used to remove the initial complex, and thereafter the preparative ultracentrifuge or M.S.E. centrifuge is utilised. The resultant products, although less densely packed, are cleaner and more easily re-dispersed.

Oxygen-free conditions are therefore essential to avoid degradation of amylose during fractionation. This can be achieved by passing nitrogen (or hydrogen [7a]) through the

TABLE 2. *β-Amylolysis limits of amylose samples.*

	Laboratory-prepared starch				Commercial starch			
Prep. of sample in N_2	Sample †	% of total amylose	$\overline{D.P.}$	β-Amylolysis limit *	Sample †	% of total amylose	$\overline{D.P.}$	β-Amylolysis limit *
Aq. leaching at 70°	F 7 ‡	40	1800	100	F 5	40	2400	100
Aq. leaching at 98°	—	80	2700	86	—	—	—	—
Dispersion of granule	F 1 ‡	100	3200	77	F 4	100	2500	95

* Expressed as % conversion into maltose. † Sample number in Table 1 where appropriate. ‡ Further enzymic experiments on these fractions have been described by Cowie, Fleming, Greenwood, and Manners (*J.*, in the press).

TABLE 3. *Analysis of fractionation products.*

Product	% of total weight [a]	Iodine affinity	% of amylose	$[\eta]$ in M-KOH	$10^{13}S_0$ [b]
Whole starch	100	4·03	20·7	—	—
(a) *Precipitates*					
Thymol complex	41	14·2	74	—	—
Butanol complex 1	—	17·5	90·3	—	—
,, 2	—	19·0	97·5	—	—
,, 3	15 *	19·5 †	100	440	12·5
(b) *Materials in supernatant liquors from*:					
Thymol complex	50	0·16	0·82	180	200
Butanol complex 1	10	0·4	2·05	76	11·3
,, 2	5	7·8	40	—	—
,, 3	2	2·0	10·25	—	—

[a] Estimated for (a) by hydrolysis of aliquot parts and estimation of liberated glucose and (b) by direct weighing of freeze-dried product. Losses are mechanical. [b] Sedimentation constant in c.g.s. units at infinite dilution obtained by graphical extrapolation from $S = f(c)$.
* A further 5% was used in analysis of butanol complexes 1 and 2.
† Value constant on further recrystallisation.

fractionation medium, which should preferably be on a small scale (*i.e.*, <500 ml.). (The results for small- and large-scale preparations in Table 1 indicate that oxygen-free conditions are more easily maintained in small-scale preparations. Also the length of time needed to centrifuge the thymol-complex is short.)

Anti-oxidants (*e.g.*, *N*-phenyl-2-naphthylamine and quinol), added to the fractionation medium in the presence of air, did not minimise oxidative degradation (cf. F2, F12, and F13; Table 1).

Other Precipitants and Fractionation Methods.—As already reported,[1] the most effective method of fractionating potato starch involved complete disruption of the granular structure, followed by precipitation of the amylose component by a polar organic molecule. Many complex-forming agents have been used, but thymol followed by butan-1-ol is a very satisfactory combination.

Higginbotham and Morrison [8] studied the use of butan-1-ol, pyridine, and *iso*pentyl

[7] Greenwood and Robertson, *J.*, 1954, 3769.
[7a] Baum and Gilbert, *Chem. and Ind.*, 1954, 489.
[8] Higginbotham and Morrison, *Shirley Inst. Mem.*, 1948, **22**, 141.

alcohol, and concluded that pyridine and butanol were comparable but *iso*pentyl alcohol was not so efficient. Results showing the effect of pyridine [8] and pentan-1-ol [9] as initial precipitants (F9 and F10; Table 1) suggest that, for potato starch, pyridine is an inefficient precipitant, yielding an amylopectin only 96·4% pure. Pentan-1-ol, however, is comparable to thymol, and a good initial separation of the components is obtained.

Starch subjected to pre-treatment with potassium hydroxide (a method suggested [10] for fractionating starches which are difficult to disperse) yielded only slightly degraded amylose. The fact that potato starch is relatively easy to swell and disperse may account for this. However, unpublished results [11] indicate that the method is also satisfactory for cereal starches.

Fractionation of Commercial Potato Starch.—Values reported for the $\overline{\text{D.P.}}$ of potato amylose have varied considerably.[3] With the exception of Husemann and Bartle's results,[12] none has been as large as our own values.[4] This could be attributed to degradation during isolation, or fractionation, or during the formation of derivatives. In our work, the latter possibility has been eliminated by studying the free component. However, previous investigators have often used commercial starch samples, so we examined such a starch.

When best-quality commercial potato starch was fractionated under *oxygen-free* conditions, the resultant amylose had a $\overline{\text{D.P.}}$ of only 2500 (F4 in Table 1). Thus commercial extraction of starch appears to degrade the amylose. This fact, together with oxidative degradation, probably accounts for the lower reported values of $\overline{\text{D.P.}}$ (A fractionation in the presence of air might be expected to result in an amylose of $\overline{\text{D.P.}}$ ~1700 before preparation of derivatives.)

Aqueous leaching of the commercial starch at 70° also gave amylose of $\overline{\text{D.P.}}$ 2400, and this value was unchanged when the granule was subsequently dispersed at 98° (see Table 1). This behaviour is completely different from that of laboratory-prepared samples,[1] and suggests that in the commercial samples all the amylose is equally accessible.

Uniformity of Structure of Amylose.—Our aqueous-leaching experiments [1] suggest that in potato starch there may be two amylose fractions, (1) easily accessible material of relatively low $\overline{\text{D.P.}}$ and (2) a fraction of higher $\overline{\text{D.P.}}$ requiring disruption of the granule before isolation. There is the possibility that these fractions may also differ in *structure*.[3] Although physical evidence shows that their iodine affinities are identical, and the same ln M *versus* ln $[\eta]$ relationship holds within experimental error, the $\overline{\text{D.P.}}$'s are so large that chemical methods are not satisfactory. However, β-amylase will degrade a linear amylose molecule completely to maltose, whilst its hydrolytic action stops at any branch-points or other anomaly.[3] Experiments carried out in collaboration with Mr. I. D. Fleming showed that the β-amylolysis limits of the different amylose fractions varied considerably (Table 2).

For laboratory-prepared starches, the complete degradation of the amylose leached at 70° suggests that this short-chain material is completely linear. Extraction at higher temperatures gives amylose which is incompletely hydrolysed, the amount of resistant material increasing with increase in temperature and consequent disruption of the granule. The probable nature of this barrier to β-amylolysis will be discussed elsewhere, but it appears to be associated with disruption of the granule and hence some branching is not improbable.[3]

The leaching and β-amylolysis results for the commercial starch differ greatly. All the amylose products were of virtually the same size, and, whilst that leached at 70° was again linear, the product of a conventional dispersion was also nearly completely hydrolysed.

[8] Schoch in Radley, "Starch and its Derivatives," Chapman and Hall, London, 1953, Vol. I, p. 123.
[10] Potter, Silveira, McCready, and Owens, *J. Amer. Chem. Soc.*, 1953, **75**, 1335.
[11] Arbuckle and Greenwood, unpublished experiments.
[12] Husemann and Bartle, *Makromol. Chem.*, 1956, **18—19**, 342.

Analysis of the "Sub-fractions" obtained during Fractionation.—The granule may contain fractions with properties intermediate between those of amylose and amylopectin.[3] In an attempt to identify such material, a careful analysis was made of all the products from a fractionation of a laboratory-prepared starch, especially the solids from the mother-liquors obtained from recrystallisation of amylose. The results are shown in Table 3. The weight of material in the supernatant liquors decreased regularly and the iodine affinity increased generally. With the exception of the solid from the supernatant liquor from butanol complex 2, the iodine-binding curves were identical in character with those previously reported for a similar analysis of *Hevea brasiliensis* starch.[7] Examination of the thymol complex in the ultracentrifuge revealed an apparently *homogeneous* fraction, although it contained about one-third of amylopectin. Amylopectin normally has a sedimentation constant about twenty times larger than amylose, but the amylopectin product isolated on reprecipitation of the thymol complex had a value equivalent to that for amylose itself. Without further evidence, it is impossible to decide whether there are also two amylopectin fractions of widely differing $\overline{D.P.}$, or whether this "thymol-amylopectin" has a different structure, although it has similar iodine-binding properties to amylopectin. Experiments are in progress to investigate this. Recrystallisation of the amylose apparently results in the elimination of branched material and presumably also short-chain amyloses, although the latter are difficult to detect by potentiometric iodine titration. With the possible exception of the "thymol-amylopectin," no major component has been detected which might be an intermediate between amylose and amylopectin.

The authors thank Professor E. L. Hirst, F.R.S., for his interest, and Mr. N. J. Philip for some experimental assistance, also the Rockefeller Foundation for financial support, and Messrs. Brown and Polson, Ltd., for a generous supply of commercial potato starch.

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[*Received, July 1st,* 1957.]

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933. *The Effect of Solvents on the Ionisation of Organic Halides. Part V.*[1] *Ionisation in Mixed Solvents.*

By Alwyn G. Evans, I. H. McEwan, and J. H. Thomas.

The ionisation of triphenylmethyl chloride in *m*-cresol–benzene and –hexane, and of tri-*p*-tolylmethyl chloride in *m*-cresol–benzene, –hexane, and –acetic acid has been investigated spectrophotometrically.

We have extended work on the ionisation of triarylmethyl halides in *m*-cresol[1a] to the systems listed in the Summary.

Experimental and Results

Materials.—*m*-Cresol (Hopkin and Williams) was purified as described earlier.[1a] Triphenylmethyl chloride and tri-*p*-tolylmethyl chloride were obtained as described by A. G. Evans, Jones, and Osborne.[2] "AnalaR" acetic acid was purified by Eichelberger and La Mer's method.[3] It was refluxed for 10 hr. with 1% w/w of chromium trioxide, then fractionated between 117·5—118·5°, refluxed for 10 hr. with triacetyl borate, and finally fractionated; the fraction of b. p. 118·1° was collected (b. p. 118·1°/758 mm., f. p. 16·60°; lit.[4]: b. p. 118·1°, f. p. 16·58—16·60°). "AnalaR" benzene was kept over sodium wire and then fractionated from either phosphoric oxide or sodium. The fraction of b. p. 80·0—80·5° was collected. Benzene purified by both methods gave the same results. Hopkin and Williams's hexane (low in

[1] (*a*) Part III, Evans, McEwan, Price, and Thomas, *J.*, 1955, 3098; (*b*) Part IV, Evans, Price, and Thomas, *Trans. Faraday Soc.*, 1955, **52**, 332.
[2] A. G. Evans, Jones, and Osborne, *Trans. Faraday Soc.*, 1954, **50**, 16.
[3] Eichelberger and La Mer, *J. Amer. Chem. Soc.*, 1933, **55**, 3633.
[4] Timmermans, "Physico-Chemical Constants of Organic Compounds," Elsevier, 1950, p. 380.

FIG. 1.

▲ Triphenylmethyl chloride concn. $1{\cdot}581 \times 10^{-4}$ mole $l.^{-1}$ at 16°. *m*-Cresol mole fraction 1·0.
× Triphenylmethyl chloride concn. $4{\cdot}872 \times 10^{-4}$ mole $l.^{-1}$ at 15°. *m*-Cresol mole fraction 0·772. Benzene mole fraction 0·228.
Y Triphenylmethyl chloride concn. $22{\cdot}41 \times 10^{-4}$ mole $l.^{-1}$ at 15°. *m*-Cresol mole fraction 0·602. Benzene mole fraction 0·398.
△ Triphenylmethyl chloride concn. $14{\cdot}83 \times 10^{-4}$ mole $l.^{-1}$ at 15°. *m*-Cresol mole fraction 0·689. Hexane mole fraction 0·311.
□ Tri-*p*-tolylmethyl chloride concn. $1{\cdot}521 \times 10^{-5}$ mole $l.^{-1}$ at 19°. *m*-Cresol mole fraction 1·0.
○ Tri-*p*-tolylmethyl chloride concn. $1{\cdot}521 \times 10^{-5}$ mole $l.^{-1}$ at 19°. *m*-Cresol mole fraction 0·953. Benzene mole fraction 0·047.
◐ Tri-*p*-tolylmethyl chloride concn. $4{\cdot}470 \times 10^{-5}$ mole $l.^{-1}$ at 19°. *m*-Cresol mole fraction 0·286. Benzene mole fraction 0·714.
⅄ Tri-*p*-tolylmethyl chloride conc. $2{\cdot}98 \times 10^{-3}$ mole $l.^{-1}$ at 19°. Acetic acid mole fraction 1·0.
● Tri-*p*-tolylmethyl chloride concn. $6{\cdot}143 \times 10^{-5}$ mole $l.^{-1}$ at 21°. *m*-Cresol mole fraction 0·190. Acetic acid mole fraction 0·810.

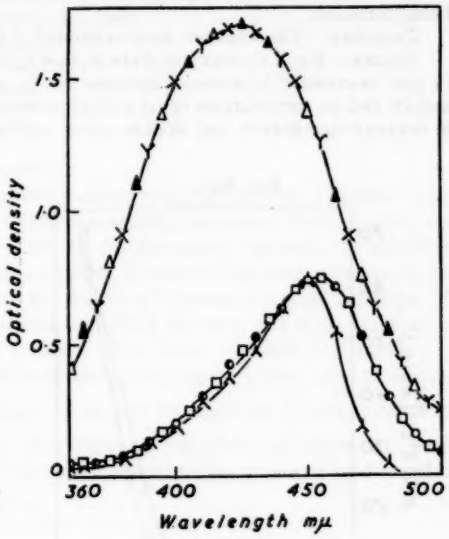


FIG. 2(*a*).

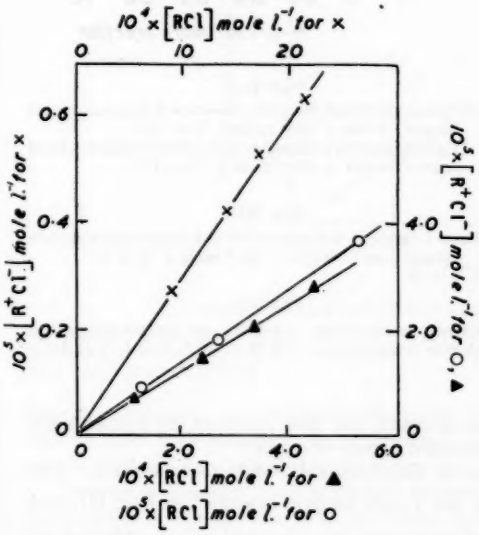


FIG. 2(*b*).

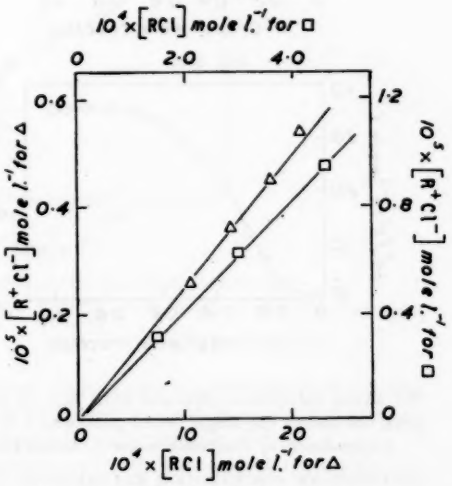


FIG. 2(*a*).

× Triphenylmethyl chloride in *m*-cresol (mole fraction 0·439)–benzene (mole fraction 0·561) at 15°.
○ Tri-*p*-tolylmethyl chloride in *m*-cresol (mole fraction 0·286)–benzene (mole fraction 0·714) at 15°.
▲ Tri-*p*-tolylmethyl chloride in *m*-cresol (mole fraction 0·079)–acetic acid (mole fraction 0·921) at 18°.

FIG. 2(*b*).

△ Triphenylmethyl chloride in *m*-cresol (mole fraction 0·370)–hexane (mole fraction 0·630) at 15°.
□ Triphenylmethyl chloride in *m*-cresol (mole fraction 0·641)–hexane (mole fraction 0·386) at 15°.

aromatic compounds) was purified in the same way as benzene, the fraction of b. p. 68—69° being collected.

Procedure.—The solutions were examined as described in Part III.

Spectra.—Fig. 1 shows typical absorption spectra (*a*) for solutions of triphenylmethyl chloride in pure *m*-cresol,[18] in *m*-cresol–benzene and in *m*-cresol–hexane, scaled to give the same peak-height, and (*b*) for solutions of tri-*p*-tolylmethyl chloride in pure *m*-cresol, in *m*-cresol–benzene, in *m*-cresol–acetic acid, and in pure acetic acid scaled similarly. The shape of the spectrum in

FIG. 3(*a*).

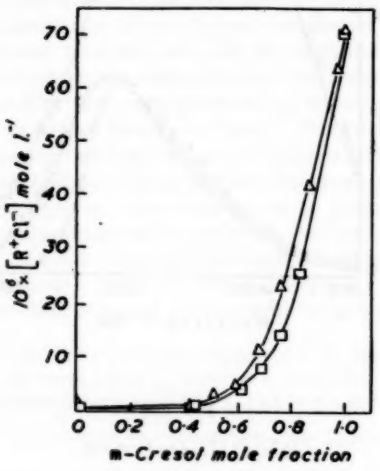


FIG. 3(*c*).

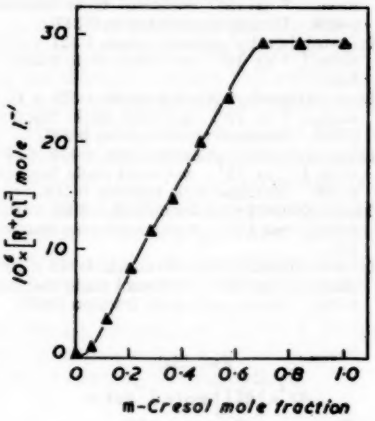


FIG. 3(*b*).

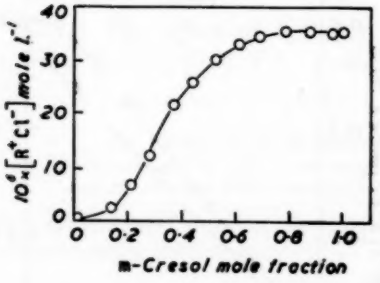


FIG. 3(*a*).

△ Triphenylmethyl chloride in *m*-cresol–benzene (total concn. $1{\cdot}864 \times 10^{-4}$ mole $l.^{-1}$) at 15°.

□ Triphenylmethyl chloride in *m*-cresol–hexane (total concn. $1{\cdot}841 \times 10^{-4}$ mole $l.^{-1}$) at 15°.

FIG. 3(*b*).

m-Cresol–benzene solution of tri-*p*-tolylmethyl chloride (total concn. $3{\cdot}531 \times 10^{-5}$ mole $l.^{-1}$) at 15°.

FIG. 3(*c*).

m-Cresol–acetic acid solution of tri-*p*-tolylmethyl chloride (total concn. $= 2{\cdot}94 \times 10^{-4}$ mole $l.^{-1}$) at 18°.

the mixed solvents is identical with that in pure *m*-cresol, and does not have the usual double peak but shows the single broad peak which is obtained in pure *m*-cresol.[18]

Dependence of Carbonium-ion Concentration on Triarylmethyl Halide Concentration.—The carbonium-ion concentration was calculated by the $\int D_\lambda d\lambda$ method described in Part III, and in Fig. 2 is plotted against the concentration of un-ionised triarylmethyl halide, obtained by subtracting the ionised from the total triarylmethyl chloride concentration. These good straight lines show that ionisation leads to the formation of ion pairs.

Dependence of Carbonium-ion Concentration on m-*Cresol Concentration.*—Figs. 3*a*, 3*b*, and 3*c* show the effect of changing the *m*-cresol concentration on the carbonium-ion concentration. The mole fractions are calculated on the basis of monomeric molecules.

Cryoscopic Measurements on the m-*Cresol–Acetic Acid System.*—The depression of the freezing point of acetic acid by *m*-cresol, measured in the normal way, shows that in this system the *m*-cresol exists as monomer (Table).

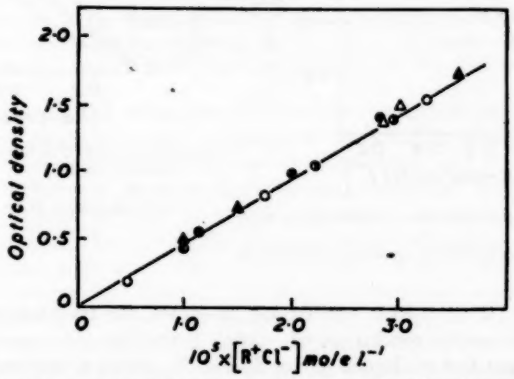
Cryoscopic determination of the molecular weight of m-*cresol in acetic acid.* (*Calc. for* C_7H_8O; *M*, 108).

m-Cresol (g./1000 g. of acetic acid)	*m*-Cresol (mole fraction)	Δt	*M*
78·16	0·04165	2·71°	111
21·50	0·0118	0·79	107
33·21	0·01811	1·22	106

Discussion

Measurement of Carbonium-ion Concentration.—For triphenylmethyl chloride, the addition of *m*-cresol to a hexane or benzene solution markedly increased the ionisation up to a value of 38% in pure *m*-cresol (Fig. 3*a*). For tri-*p*-tolylmethyl chloride, the addition of *m*-cresol to a benzene or acetic acid solution rapidly increased the ionisation up to an *m*-cresol mole fraction of about 0·7, after which the degree of ionisation is constant (Figs. 3*b* and 3*c*). This constancy shows that in solutions for which the *m*-cresol mole fraction is >0·7 the tri-*p*-tolylmethyl chloride is fully ionised. For these solutions our method [1a] of determining the carbonium-ion concentration gives a value which is the same to within ±5% of that corresponding to 100% ionisation. This fact justifies our $\int D_\lambda d\lambda$ method of obtaining the ionic concentrations. Further, this region of complete ionisation has been obtained for different total tri-*p*-tolylmethyl chloride concentrations, and in Fig. 4 we plot

Fig. 4.



D_λ values for completely ionised solutions of tri-*p*-tolylmethyl chloride.

m-Cresol (mole fraction)	▲ 0·953	● 0·862	△ 0·772	◑ 0·843	◐ 0·701	○ 1·0
Benzene (mole fraction)	0·047	0·138	0·228	—	—	—
Acetic acid (mole fraction) ...	—	—	—	0·157	0·299	—

the optical density, D_λ, of these completely ionised solutions of tri-*p*-tolylmethyl chloride against their carbonium-ion concentration. The very good straight line obtained demonstrates that for the optical-density range used, Beer's law is accurately obeyed.

Ionisation Equilibria.—The plot of carbonium-ion concentration against the un-ionised halide gives a straight line (Fig. 2), which shows that ionisation leads to the formation of ion pairs [according to eqn. (1)]. For those tri-*p*-tolylmethyl chloride solutions in which ionisation is complete, it is, of course, impossible to tell by this spectrophotometric method what proportion of the ions are present as ion pairs or as free ions.

Order of Ionisation in m-*Cresol.*—Any analysis of the results obtained in the *m*-cresol–benzene and *m*-cresol–hexane systems is rendered difficult by the considerable complexing to dimers and higher polymers that is a feature of hydroxylic groups in non-polar solvents like benzene and hexane.[5] Thus, when log $[R^+Cl^-]/[RCl]$ is plotted against log [*m*-cresol]

[5] Coggeshall and Saier, *J. Amer. Chem. Soc.*, 1951, **73**, 5416.

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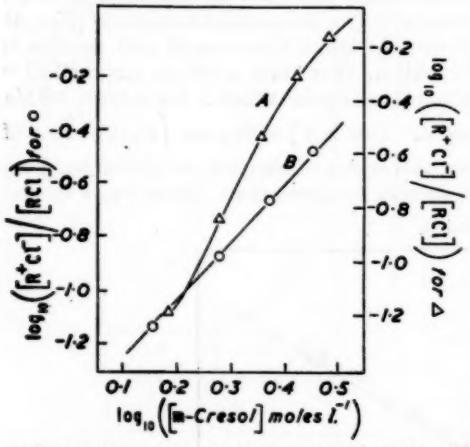
for the ionisation of tri-*p*-tolylmethyl chloride in *m*-cresol–benzene and *m*-cresol–hexane, under conditions of <25% ionisation (*i.e.* of *m*-cresol mole fraction <0·2; see, *e.g.*, Fig. 5, curve *A*), the slope varies continuously over the concentration range, and this could be due to the various equilibria existing between *m*-cresol monomer and polymer in these inert solvents, and to their differing powers of solvation.

There is considerable evidence, however, that when dissolved in oxygenated solvents, where solvent–hydroxyl complexes may arise (*e.g.* benzoic acid in acetic acid [6]), *m*-cresol is monomeric. We have now shown cryoscopically that *m*-cresol is monomeric in acetic acid up to a mole fraction of 0·04. (Recent work by Boozer, Robinson, Soldatos, Trisler, and Wiley uses the fact that formic and chloroacetic acids are monomeric in acetic acid.[7])

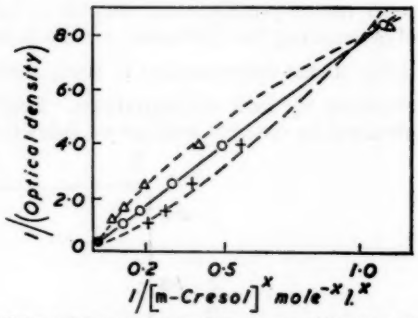
FIG. 5.



○ Tri-*p*-tolylmethyl chloride in *m*-cresol–acetic acid at 20°.

△ Tri-*p*-tolylmethyl chloride in *m*-cresol–benzene at 20°.

FIG. 6.



Tri-*p*-tolylmethyl chloride in *m*-cresol/acetic acid solution at 20°.

△, $x = 2·5$; ○, $x = 2·0$; +, $x = 1·5$; ● Intercept calculated from 1/[total RCl] × ε.

The plot of log [R^+Cl^-]/[RCl] against log [*m*-cresol] for tri-*p*-tolylmethyl chloride in *m*-cresol–acetic acid under conditions of <25% ionisation (*i.e.*, *m*-cresol mole fraction <0·2) gives a straight line of slope 2 (curve *B*, Fig. 5), showing that in these mixtures the order in *m*-cresol for the production of ion pairs is 2·1 ± 0·1. Confirmation of this is obtained from the Benesi–Hildebrand plot [8] (Fig. 6) when $1/D_{\lambda,\max.}$ is plotted against $1/[m\text{-cresol}]^x$ over the same range of *m*-cresol concentration for a constant total tri-*p*-tolylmethyl chloride concentration of $8·477 \times 10^{-5}$ mole $l.^{-1}$. [The intercept on the $1/D_{\lambda,\max.}$ axis has been evaluated from the extinction coefficient ε ($4·8 \times 10^{+4}$) of the ion in *m*-cresol (see Fig. 4).] When $x = 2$, a good straight line is obtained, but when $x = 1·5$ or 2·5, deviation from linearity is evident.

Thus in *m*-cresol–acetic acid solution of tri-*p*-tolylmethyl chloride (mole fraction <0·2) we have an ionisation equilibrium of the type

$$(p\text{-Me}\cdot C_6H_4)_3CCl + 2m\text{-}CH_3\cdot C_6H_4\cdot OH \underset{b}{\overset{a}{\rightleftharpoons}} \{(p\text{-Me}\cdot C_6H_4)_3C^+Cl^-\}_{solv.} \quad . \quad (4)$$

in which 2 *m*-cresol molecules are involved in the solvation of the ion pair. The thermodynamic constants for this equilibrium at 21° are as follows, for acetic acid solution: K_4 (mole-fraction units), 8·9; $\Delta G°_{4a}$, −1·3 ± 0·2 kcal. $mole^{-1}$.

[6] Lassetre, *Chem. Rev.*, 1938, **20**, 259.
[7] Boozer, Robinson, Soldatos, Trisler, and Wiley, *J. Amer. Chem. Soc.*, 1956, **78**, 3428.
[8] Benesi and Hildebrand, *ibid.*, 1948, **70**, 2703.

Hudson and Saville,[9] in their study of the ionisation of triphenylmethyl chloride in carbon tetrachloride solutions of phenol, have tentatively suggested that the order in phenol for the ionisation is 2 at very low phenol concentration.

We thank the University College, Cardiff, for a British Nylon Spinners Post-graduate Scholarship (to I. H. McE.).

UNIVERSITY COLLEGE, CARDIFF. [*Received, May 30th,* 1957.]

[9] Hudson and Saville, *J.*, 1955, 4130.

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934. *The Mechanism of the Reaction of Aryl* iso*Cyanates with Alcohols and Amines. Part VI.*[1] *Preliminary Investigations with Amines: Complex-formation by Amines and Ureas in Benzene Solution.*

By JOHN W. BAKER and D. N. BAILEY.

Early in a kinetic investigation of the reaction Ar·NCO + NH_2R ⟶ Ar·NH·CO·NHR in dry benzene solution at 20° (following papers) it was found that the ureas formed have pronounced catalytic effects. The solubilities of these products are greatly affected by the concentration of NH_2R, and, to a smaller extent, by that of Ar·NCO and of a tertiary base catalyst, present in the reaction media. As an essential preliminary to an analysis of the complex kinetics of the reaction these solubility changes have been quantitatively determined, and their nature is briefly discussed.

EARLIER work (Parts I—V)[1] demonstrated that the "spontaneous" reaction between aryl *iso*cyanates and alcohols is more complicated than that represented by the simple bimolecular mechanism Ar·NCO + ROH ⟶ Ar·NH·CO·OR and involves the attack of one molecule of the alcohol upon an initially (and reversibly) formed **1 : 1** molecular complex of alcohol and *iso*cyanate. In the presence of a tertiary base, a base-catalysed reaction is superimposed which similarly involves alcohol attack on an initially formed 1 : 1 molecular complex of the *iso*cyanate and the tertiary amine. Such mechanisms were later confirmed by independent results.[2] In the "spontaneous" reaction weak catalysis by the urethane product was also demonstrated.[1]

In extension of these investigations to the *iso*cyanate–amine reaction it early became apparent that the formation of heterogeneous media, due to crystallisation of the much less soluble ureas formed, introduces serious complications, especially when it was established that these products have much more pronounced catalytic effects than do the urethanes in the corresponding reaction with alcohols. When attempts were made to standardise such autocatalysis by working in media saturated with the urea product, it was found that the solubilities of the ureas are greatly affected by the concentration of the reactant amine and, to a much smaller extent, by the *iso*cyanate and tertiary amine concentrations in the media. In order to interpret the complicated kinetics in our study of the amine–*iso*cyanate reaction it was, therefore, necessary to obtain solubility data for the different urea products in the presence of the various amines and *iso*cyanates used in the investigation.

Such data are recorded in Tables 1—4. Rigid exclusion of moisture was maintained throughout, the solubilities being determined by direct weighing from saturated solutions in equilibrium with undissolved solid at 20·0°. The following abbreviations are used: Carb. A = NHPh·CO·NH·C_6H_4·CO_2Et-*p*; Carb. B = NHPh·CO·NH·C_6H_{11} (C_6H_{11} = *cyclo*hexyl); Carb. C = $CO(NHPh)_2$; Carb. D = NHPh·CO·NH·C_6H_4·OMe-*p*. All concentrations are in mole $l.^{-1}$.

[1] Parts I—V, J. W. Baker *et al.*, *J.*, 1947, 713; 1949, 9, 19, 24, 27.
[2] Dyer, Taylor, Mason, and Samson, *J. Amer. Chem. Soc.*, 1949, **71**, 4106.

From plots of these results it was possible, assuming that the increases in solubility due to any one entity are additive, to determine the saturation concentration of the catalytic urea product at any stage in a reaction between an *iso*cyanate and an amine. Within the experimental concentration ranges employed, the dominant effect is that due to the presence of the reactant amine, and neglect of the effect of both *iso*cyanate (~0·07M) and tertiary amine (0·003—0·3M) concentrations involves an error of only ~0·5% in the calculated saturation concentration of the urea, an error too small to be significant. The important point emerges that, whilst, as reaction proceeds, loss of *iso*cyanate has little effect on the saturation concentration of the catalytic urea product, the corresponding fall in reactant amine concentration is highly significant in this respect.

TABLE 1. *Solubility of Carb. A in dry benzene solutions of* (a) NEt_3, (b) NH_2Ph, (c) *p*-$NH_2{\cdot}C_6H_4{\cdot}CO_2Et$, *and* (d) Ph·NCO, *at* 20°.

(*a*) 10^3[NEt_3]	0	0·99	2·49	4·99	9·99	24·97	34·95	49·94	99·88
10^3[Carb. A]	1·65	1·5	1·6	1·8	2·1	3·3	3·9	4·6	6·1
(*b*) 10^3[NH_2Ph]	0	5·0	10·0	50·0	75·0	100·0			
10^3[Carb. A]	1·65	1·5	1·6	3·3	5·0	6·7			
(*c*) 10^3[*p*-$NH_2{\cdot}C_6H_4{\cdot}CO_2Et$]	0	2·63	5·26	10·52	21·04	29·46	33·66	42·08	
10^3[Carb. A]	1·65	3·0	4·0	6·9	11·7	15·3	17·9	22·6	
(*d*) 10^3[PhNCO]	0	5·0	10·0	25·0	50·0	75·0			
10^3[Carb. A]	1·65	1·64	1·69	1·71	1·92	2·18			

TABLE 2. *Solubility of Carb. C in dry benzene solutions of* (a) NH_2Ph *and* (b) Ph·NCO, *at* 20°.

(*a*) 10^3[NH_2Ph]	0	25·02	50·05	75·07	100·1
10^3[Carb. C]	0·424	0·6	1·0	1·3	2·2
(*b*) 10^3[Ph·NCO]	0	5·00	10·00	25·03	50·05	75·08
10^3[Carb. C]	0·424	0·429	0·424	0·448	0·481	0·537

TABLE 3. *Solubilities of various* NN′*-disubstituted ureas in dry benzene solutions of aniline at* 20°.

10^3[NH_2Ph]	0	5·0	10·0	25·0	50·0	75·0	100
10^3[Carb. A]	1·65	1·5	1·6	—	3·3	5·0	6·7
10^3[Carb. B]	2·91	3·30	3·41	4·22	5·78	7·57	9·80
10^3[Carb. C]	0·42	—	—	0·6	1·0	1·3	2·2
10^3[Carb. D]	0·54	0·59	0·67	0·82	1·19	1·68	2·39

TABLE 4. *Dependence of solubility of Carb. A in dry benzene at* 20° *on* (a) *p*-$NH_2{\cdot}C_6H_4{\cdot}CO_2Et$, (b) NH_2Ph, *and* (c) NEt_3.

Reagent	K_b	Increase in solubility (M) of Carb. A due to [reagent] = 0·5M	1·0M
a	$2·9 \times 10^{-12}$ *	0·0237	(0·047)
b	$4·6 \times 10^{-10}$	0·00165	0·00505
c	$5·65 \times 10^{-4}$	0·00295	0·00445

* For Me ester.

These solubility dependences clearly point to complex formation between the entities present in solution, most probably due to hydrogen bonding, of which many types are possible in the systems examined, *e.g.*, $>C{:}O{\rightarrow}H{-}N<$, $\geqslant N{\rightarrow}H{-}N<$, $>O{\rightarrow}H{-}N<$ and, in addition, complex-formation of the type $\geqslant N{\rightarrow}C(=O)$. Such complex-formation would be favoured by the inability of the solvent benzene to associate with the various solutes.

Examination of Table 4 reveals that the basic strength of the amine is evidently not the factor mainly concerned in complex formation. The greatest solubility increase

occurs when the group CO_2Et is present in both the urea and the amine, *i.e.*, in the interaction of benzocaine (*a*) with Carb. A, the solubility of which is accurately represented by the linear relation [Carb. A] = 0·00165 + 0·0469[*p*-NH_2·C_6H_4·CO_2Et] mole $l.^{-1}$ over the range [*p*-NH_2·C_6H_4·CO_2Et] = 0 to 0·5M. The extrapolated value in 1M-solution in Table 4 (included for comparison) is derived from this relation, although a saturated solution of benzocaine itself in dry benzene at 20° is only 0·6M. Such association should occur in benzocaine itself, and, in agreement with this, cryoscopic determinations of its apparent molecular weight in benzene solution revealed that this increases from 166 (monomeric = 165·1) in very dilute solutions to 184 in 0·22M-solution, equivalent to 11·5% dimerisation.

It therefore seems most probable that the observed solubility effects are also mainly due to hydrogen-bonding association, although the number of different possibilities makes it impossible to specify the predominant type.

Experimental

Materials.—The various ureas were prepared by direct interaction of the appropriate pure dry *iso*cyanate and amine (in slight excess), either without solvent or in pure dry benzene, at room temperature, followed by repeated crystallisation from methanol and drying over phosphoric oxide in a vacuum. Thus were obtained: *N*-*p*-ethoxycarbonylphenyl-*N'*-phenyl-, m. p. 169° (Found: C, 67·6; H, 5·65; N, 9·7. Calc. for $C_{16}H_{16}O_3N_2$: C, 67·6; H, 5·7; N, 9·9%); *N*-*p*-methoxyphenyl-*N'*-phenyl-, m. p. 192°, *N*-*cyclo*hexyl-*N'*-phenyl-,[3] m. p. 184° (Found: C, 71·8; H, 8·1; N, 13·1. Calc. for $C_{13}H_{18}ON_2$: C, 71·5; H, 8·3; N, 12·8%), and *NN'*-diphenyl-urea, m. p. 239° (from acetone). Other materials were purified as described in Part VII (following paper).

Solubility Determinations.—A standard solution of the reagent (freshly distilled if liquid) in pure dry benzene was prepared by direct weighing and solutions of various concentrations were prepared from this by suitable dilution. Excess of the solid urea was stirred with 100 c.c. of the solution at 30° and the whole was then allowed to come into equilibrium with undissolved solid during 18 hr. at 20°. The saturated solution (10 c.c.) was removed through a sintered-glass filter-stick, weighed, and evaporated on a steam-bath for 90—120 min. (aniline) or 30 min. (NEt_3 and benzocaine), dried at 110° for 1 hr. to constant weight, and stored over phosphoric oxide for 0·5 hr. before weighing. Blank experiments showed that the standard procedure caused no change in weight of the urea, or of benzocaine when this was also present, and that other amines were completely removed. When phenyl *iso*cyanate was present removal of this and the solvent was effected in a vacuum over phosphoric oxide, rigid precautions for the exclusion of moisture being maintained throughout the solubility determination.

Molecular Weight of Benzocaine.—This was determined in the usual manner by cryoscopic measurements in pure dry benzene (17·66 g.: k = 5·12°).

Wt. (g.) of *p*-NH_2·C_6H_4·CO_2Et	0·1660	0·2553	0·3215	0·4339	0·5021	0·5730	0·6674	0·7278
ΔT°	0·289	0·461	0·558	0·740	0·831	0·919	1·046	1·127
M	166	(159)	166	168	173	178	182	184

Department of Organic Chemistry,
The University, Leeds.

[*Received, May 31st,* 1957.]

[3] Skita and Rolfes, *Ber.*, 1920, **53**, 1248.

935. *The Mechanism of the Reaction of Aryl* iso*Cyanates with Alcohols and Amines. Part VII.* The "Spontaneous" Reaction with Amines.*

By JOHN W. BAKER and D. N. BAILEY.

Kinetic investigations of the reaction $Ar{\cdot}NCO + NH_2R \longrightarrow Ar{\cdot}NH{\cdot}CO{\cdot}NHR$ for four *iso*cyanate–amine pairs in dry benzene solution at 20°, and with rigorous exclusion of moisture, are described. Analysis of the results shows that a product-catalysed reaction is superimposed upon a true "spontaneous" reaction, both of which follow a mechanism: $Ar{\cdot}NCO + A \rightleftharpoons$ Complex; Complex $+ NH_2R \longrightarrow$ Products; where $A = Ar{\cdot}NH{\cdot}CO{\cdot}NHR$ and NH_2R, respectively. These mechanisms are complicated by the fact that the solubility of the sparingly soluble, precipitated products decreases as the $[NH_2R]$ falls, and by supersaturation phenomena due to the fact that the rate of formation (r_f) of the product exceeds its rate of deposition (r_d) in the early stages of the reaction. Some time after deposition of the product commences, r_d becomes greater than r_f until, finally, equilibrium conditions $r_f = r_d$ are attained and the second-order plot then becomes linear. By quantitative determination of these various factors the whole course of the reactions of the various *iso*cyanate–amine pairs under varying experimental conditions is satisfactorily accounted for. The nature of the catalysis by NH_2R and $Ar{\cdot}NH{\cdot}CO{\cdot}NHR$ is discussed.

EARLY examinations of the reaction between aryl *iso*cyanates and amines to give ureas were restricted either to determination of relative velocities, derived by analysis of the products when a mixture containing one equivalent each of two different amines was allowed to compete for only one equivalent of *iso*cyanate,[1] or by weighing the urea formed when the *iso*cyanate and amine had reacted for a fixed time at a definite temperature.[2]

After the work here described was completed Arnold, Nelson, and Verbane[3] gave a preliminary account of some (unpublished) work by Craven on kinetic studies of the reaction between phenyl *iso*cyanate and some aryl primary amines in dioxan solution at 31°. The reaction was studied only in homogeneous solution before appreciable separation of the carbanilide product began. In view of the complications which we now elucidate the conclusion that "initial rates of reaction . . . show substantial variations in their dependence upon amine concentration" is readily understandable, as also is the finding that "specific examples display considerable individuality."

The analytical method for determination of aryl *iso*cyanates, and the technique developed for kinetic study of the *iso*cyanate–alcohol reaction,[4] have now been extended to detailed kinetic examination of the amine–*iso*cyanate reaction in dry benzene solution at 20° with rigid exclusion of moisture.

The mechanism: $Ar{\cdot}NCO + Base \underset{k_b}{\overset{k_i}{\rightleftharpoons}}$ Complex; Complex $+ A \xrightarrow{k_p}$ Product + Base; leading to the relation $k_{bi} = k_i k_p[Base]/(k_b + k_p[A])$, previously established for the experimentally determined second-order coefficient k_{bi} for the tertiary base-catalysed alcohol reaction ($A = ROH$),[4b] suggested that a similar relation ($A =$ base $=$ reacting amine, NH_2R) might hold for the spontaneous *iso*cyanate–amine reaction, leading to the expression $[NH_2R]/k_{bi} = 1/k_e = k_b/k_i k_p + [NH_2R]/k_i$, so that a plot of $[NH_2R]$ against $1/k_e$ would be linear. Preliminary experiments with aniline and phenyl *iso*cyanate at once showed that, although the value of k_{bi} does vary with the initial concentration of

* Part VI, preceding paper.

[1] Davis and Ebersole, *J. Amer. Chem. Soc.*, 1934, **56**, 885.
[2] Naegali, Tyabi, Conrad, and Litwan, *Helv. Chim. Acta*, 1938, **21**, 1100, 1127.
[3] Arnold, Nelson, and Verbane, *Chem. Rev.*, 1957, **57**, 47.
[4] Baker *et al.*, *J.*, (*a*) 1947, 713; 1949, (*b*), 9, (*c*) 19, 24, 37.

aniline, no such simple relation is valid. The high solubilities of arylurethanes permitted kinetic examination of the alcohol–*iso*cyanate reaction in a homogeneous medium, but the much lower solubilities of ureas cause crystallisation of these products in the early stages of the amine–*iso*cyanate reaction to give heterogeneous conditions. Satisfactory determination of unchanged *iso*cyanate (to follow the course of the reaction) is possible in such heterogeneous media by filtration through a sintered-glass micro-filter-stick attached to the end of the pipette used to remove samples, but it was soon found that the heterogeneous conditions introduce serious complications into the study of the reaction mechanism.

The disentangling of these factors and the elucidation of mechanism was achieved only by detailed analysis of a large number of experimental results obtained under widely varied experimental conditions with a number of different *iso*cyanate–amine pairs, but the resultant picture is best described by reversing this order and first summarising the nature of these complications and then discussing typical experimental results which substantiate the conclusions reached.* This paper deals only with the " spontaneous " reaction between an amine and an *iso*cyanate without addition of any *extraneous* catalyst. The base-catalysed reaction under the influence of an added tertiary base will be discussed in Part VIII (following paper).

For brevity the various systems studied are denoted as follows:

A. $Ph{\cdot}NCO + p\text{-}NH_2{\cdot}C_6H_4{\cdot}CO_2Et \longrightarrow Ph{\cdot}NH{\cdot}CO{\cdot}NH{\cdot}C_6H_4{\cdot}CO_2Et$ (Carb. A)

B. $cyclo\text{-}C_6H_{11}{\cdot}NCO + NH_2Ph \longrightarrow Ph{\cdot}NH{\cdot}CO{\cdot}NH{\cdot}C_6H_{11}$ (Carb. B)

C. $Ph{\cdot}NCO + NH_2Ph \longrightarrow (Ph{\cdot}NH)_2CO$ (Carb. C)

D. $p\text{-}MeO{\cdot}C_6H_4{\cdot}NCO + NH_2Ph \longrightarrow Ph{\cdot}NH{\cdot}CO{\cdot}NH{\cdot}C_6H_4{\cdot}OMe$ (Carb. D).

In the " spontaneous " reaction between an *iso*cyanate and an amine in dry benzene solution the following factors influence the experimentally determined rate of reaction:

(1) Direct interaction between *iso*cyanate and amine to give the product.

(2) In agreement with Craven's finding (see ref. 3), the urea product is a much more effective catalyst for this reaction than is the very weakly catalytic urethane in the *iso*cyanate–alcohol reaction.

(3) The solubility of the product is greater the larger is the concentration of reacting amine from which it is formed. This factor is very large in system A, the solubility of Carb. A in a benzene solution of benzocaine being increased about 15-fold when the benzocaine concentration is increased from 0 to 0·5M.[5] Thus as the reaction progresses the amount of catalytic urea formed increases but, because the concentration of reacting amine is continually falling, so also is the solubility of this product in the reaction medium.

(4) The low solubilities of the ureas cause crystallisation of the product in the early stages of reaction, but, in homogeneous solutions initially containing no urea, considerable supersaturation builds up. Even in heterogeneous media, in the presence of the solid urea, the initial rate of product deposition (r_d) from the reaction medium is slower than its rate for formation (r_f) and it is only in the latter stages that the equilibrium $r_f = r_d$ is established, and the urea concentration (although still greater than the true solubility) then remains approximately constant for the remainder of the reaction because the reactant amine concentration has become small and changes little in these final stages of reaction. The second-order velocity coefficient then attains constancy.

(5) Both the true " spontaneous " and the product-catalysed reactions are not true second-order reactions but are both of the form already established for the *iso*cyanate–alcohol reaction, *viz.*:

*iso*Cyanate + C $\rightleftharpoons$ Complex, followed by

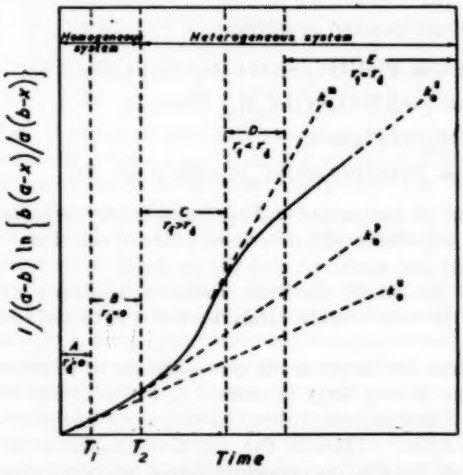
Complex + $NH_2R \longrightarrow$ Products (C = NH_2R or urea)

* For a detailed discussion see D. N. Bailey, Thesis, Leeds, 1955.

[5] Part VI, preceding paper.

The superimposition of all these factors means that the whole second-order plot for the reaction is a shallow S-shaped curve, merging finally into a linear plot, the general type of which is indicated schematically in the Figure. Depending on the speed of reaction, the catalytic effect of the product, and the supersaturation phenomena indicated in (4) above, the experimental plot for any single experiment may be represented by any one section *A*, *B*, *C*, *D*, or *E* of this curve or, of course, any combination of consecutive sections, and examples of all such plots were observed with various reactant pairs under suitable experimental conditions.

The results are discussed in terms of the apparent instantaneous second-order rate coefficients k_0 at different stages of the reaction. Such instantaneous k_0 values were determined either by drawing tangents to the second-order plot at the required reaction points, or by " small interval " determinations in the required region, whence an average value of the coefficient for mean concentrations of amine and product is obtained over a range where changes in these concentrations are very small. The two methods gave consistent values. Specific k_0 values, shown in the Figure, are defined as follows: k_0^u = the value of the second-order rate coefficient in homogeneous medium at the equilibrium



Schematic second-order plot for the reaction Ar·NCO + R·NH$_2$ ⟶ Ar·NH·CO·NHR *in both homogeneous and heterogeneous media.*

T_1 = *Time when product formed saturates the medium.*
T_2 = *Time when deposition of solid product begins.*

saturated [Ar·NH·CO·NHR]; k_0^p is the value at the time when product begins to crystallise: k_0^m is the maximum value observed after crystallisation has commenced, and k_0^s is the final, constant value in heterogeneous media when an approximately constant concentration of product is maintained. All k_0 values are in mole^{-1} l. sec.$^{-1}$.

The reaction of an *iso*cyanate with amines is much more rapid than is that with alcohols, and the rate increases with increase in the basic strength of the amine. Preliminary investigation to find an amine of suitable basic strength to give rates convenient for measurement over a wide range of amine concentration suggested system A as one suitable for initial study.

I(a). *System A in Dry Benzene in Initially Homogeneous Solution.*—The absence of side reactions was shown by the observation that the product Carb. A had m. p. 168—169°, unchanged by subsequent crystallisation, and gave correct analytical figures. The absence of reversibility was proved by the observation that no phenyl *iso*cyanate could be detected, by the sensitive analytical method used, when a saturated solution of Carb. A in dry benzene was kept at 20° for 196 hours. When a benzene solution of phenyl *iso*cyanate (0·07M), also saturated with Carb. A, was kept for five days at 20° no change in the *iso*cyanate concentration was detected. Hence, under the reaction conditions used, there is no further reaction between *iso*cyanate and Carb. A to give the biuret.

The choice of system A proved fortunate since, with varying initial concentration of the reactant amine, benzocaine, it revealed all the possible types of rate curves depicted in the Figure, although other systems were found to be more satisfactory for detailed investigation of certain sections of the curve. Table 1 summarises the results obtained in solutions where the initial [Ph·NCO] = 0·0710M but the [benzocaine] is varied: the values of k_0 are those obtained from the slopes of the approximately linear portions of the second-order plots.

The second-order plots of Nos. 6 and 7 are the full S-shaped type, whilst those for Nos. 1—5 are in the *A*, *B*, *C* sections of the Figure. The value of k_0 increases with time, *i.e.*, as the [Carb. A] increases, and the larger is the initial [benzocaine] the larger is k_0 at any

TABLE 1. *Reaction between* p-$NH_2{\cdot}C_6H_4{\cdot}CO_2Et$ *and* Ph·NCO (0·0710M) *in dry benzene at* 20°.

No.	10 × Initial [benzocaine] (M)	10^5k_0	When deposition begins: % reaction	When deposition begins: 10^3[Carb. A] = C * (M)	Solubility † 10^3 [Carb. A] at point of deposition = S(M)	Supersaturation of Carb. A = $(C - S)$ (10^{-3}M)
1	5·091	—	57	4·08	2·46	1·62
2	4·018	11·3	43	3·03	1·98	1·05
3	3·215	10·4	31	2·19	1·63	0·56
4	2·679	9·47	32	2·31	1·36	0·95
5	1·339	5·71	39	2·78	0·68	2·10
6	0·669	5·21	20	1·35	0·40	0·95
7	0·335	4·59	22	0·76	0·28	0·48

* Determined from % reaction. † From data in Part VI.

given time. True linearity is not achieved until some time after crystallisation of Carb. A has begun. At this point the solution is supersaturated with product, but the figures in the last column of Table 1 indicate the irregular nature of the deposition from initially homogeneous media. This irregularity could be visually observed: in some experiments crystals were formed in the body of the solution and steadily dropped to the bottom of the vessel; in others crystal deposition occurred on the sides of the vessel; occasionally the whole solution became suddenly filled with a fine net-work of crystals. These physical differences were reflected in the observed values of k_0 and in the form of the second-order plot.

TABLE 2. *Catalytic effects of* Ar·NH·CO·NHR *on the reaction,* Ar·NCO + NH_2R ⟶ Ar·NH·CO·NHR, *in initially homogeneous solution in dry benzene at* 20°.

Initially [Ar·NCO] = [NH_2R] = ~ 0·07M.

System	10^3[Ar·NH·CO·NHR] (M): (*a*)	(*b*)	$10^5k_0{}^a$	$10^5k_0{}^b$	$k_0{}^b/k_0{}^a$
A	0·06	0·76	1·70	9·66	5·68
B	0·01	0·34	0·171	0·955	5·5
	0·10	0·85	0·463	1·87	4 *

* Initial [NH_2Ph] = 0·5584M.

The marked catalytic effect of the product is demonstrated by the results in Table 2 which includes data from two different systems. The hypothesis that a simple autocatalytic reaction occurs was first tested and disproved. This would require $dx/dt = k_c'(a - x)(b - x)(x)$, which, by integration, gives

$$k_c' = (1/t)\{ab(a - b)\} . [a \ln \{bx/(b - x)\} - b \ln \{ax/(a - x)\}]$$

which would require a linear plot between t and the expression in square brackets. This test was applied to data obtained in many runs in homogeneous solution but in no case was a linear plot obtained.

In an attempt to standardise conditions, attention was next directed to a study of the reaction in the presence of varying excesses of added solid product, always more than

sufficient to keep the *medium* saturated with regard to product. Such conditions might be expected to eliminate sections *A*—*D* of the curve and give only the linear section *E*.

I(b). *The System A in Dry Benzene in Heterogeneous Media.*—This system was first examined by using fixed initial concentrations of *iso*cyanate and amine but varying amount of solid product. The results are in Table 3. All these runs gave *approximately*

TABLE 3. *Dependence of k_o^s on weight of undissolved Carb. A present in the medium.*

Initially: [Ph·NCO] = 0·0714M; [*p*-NH_2·C_6H_4·CO_2Et] = 0·2204M. Equilibrium saturation [Carb. A] varies throughout any one run from 0·0123 to 0·0114M.

No.	12	13	14	15
Wt. (g.) of Carb. A in excess of that (0·0700 g.) required for saturation	0·0696	0·2114	0·4244	0·8206
$10^5 k_o^s$	6·57	6·39	5·66	5·65

linear second-order plots passing through the origin, although more detailed examination sometimes revealed slight curvature [see para. III (1)]. These results definitely prove the absence of heterogeneous catalysis on the surface of the solid present. The slight fall (~20%) in the values of k_o^s observed when a very large amount of solid is present is explained in paragraph IV.

Under such saturated conditions, since the solubility of the product increases as the initial concentration of the reacting amine is increased, so also does k_o^s. This is shown by the results in Table 4. Except for experiments at very low concentrations (Nos. 20 and 21)

TABLE 4. *Variation of k_o^s with initial* [NH_2·C_6H_4·CO_2Et] *in solutions initially saturated with Carb. A.* Initial [Ph·NCO] = 0·0739M.

No.	16	17	18	19	20	21
Initial 10^3[NH_2·C_6H_4·CO_2Et] (M)	49·25	31·10	25·92	12·96	6·48	3·24
Mean 10^3 [Carb. A] (M)	24·2	15·9	13·6	7·2	4·6	3·0
$10^5 k_o^s$	12·8	9·67	8·26	6·7	5·06	4·89

where maximal experimental errors occur, a plot of k_o^s against mean [Carb. A] gives a good straight line; hence k_o^s is directly proportional to the concentration of the product. This suggests that the rate data might be satisfied by the relation $k_{bi} = k_s + k_o'$ [Carb. A], *i.e.*, by:

$$dx/dt = k_s(a - x)(b - x) + k_o'(a - x)(b - x)x, \quad . \quad . \quad . \quad \text{(i)}$$

where k_s = rate coefficient for a true " spontaneous " reaction and k_o' is the catalytic coefficient for the product, Carb A. This relation may be transposed thus: $dx/dt = k_o'(a - x)(b - x)(K + x)$ where $K = k_s/k_o'$, integration of which gives:

$$k_o't = [1/(K + a)(K + b)(b - a)][b \ln a(K + x)/K(a - x) + a \ln K(b - x)/b(K + x) + K \ln a(b - x)/b(a - x)] \quad . \quad . \quad . \quad \text{(ii)}$$

This relation would only be generally valid if both the " spontaneous " and the product-catalysed reaction were true second-order reactions, *i.e.*, if both k_s and k_o' are independent of the concentration of the reacting amine, postulates shown not to be valid by a more detailed examination of the instantaneous rate coefficients in homogeneous media.

II. *Analysis of the Variation of k_o in Homogeneous Media.*—Typical values of such instantaneous rate coefficients k_o at various points in runs in homogeneous media are given in Table 5, where only the results for the largest and smallest initial values of [NH_2R] are recorded. The intermediate values of [NH_2R] showed similar variations in k_o.

The plots of instantaneous k_o against [Carb.] are all linear, but (1) the value of the intercept on the k_o axis when [Carb.] = 0 (*i.e.*, k_s) increases and (2) the slope of the lines decreases, as the initial [NH_2R] is increased. Hence, in equation (i) the value of k_s is larger the higher is the initial concentration of reactant amine and k_o' is a function of the reciprocal of the initial concentration of reactant amine, although the concentration change *in any one experiment* is insufficient to cause detectable deviations from linearity. Thus,

although each individual run is correctly represented by the equation $k_o = k_s + k_c'$[Carb.], *both* k_s and k_c' are dependent on the initial [NH_2R]. This close similarity to the previously

TABLE 5. *Dependence of* k_o *on initial* [NH_2R] *and on* [*Carb.*] *in homogeneous solutions.*

System A. Initial [Ph·NCO] = 0·0710M.

(1) Initial [NH_2·C_6H_4·CO_2Et] = 0·5091M.						
10^3[Carb. A] (M)	2·2	3·8	10·1	16·4	24·4	32·0
10^5k_o	3·50	4·28	5·43	7·07	9·25	11·2
(2) Initial [NH_2·C_6H_4·CO_2Et] = 0·0335M.						
10^3[Carb. A] (M)	0·3	0·6	2·4	4·2	5·9	7·6
10^5k_o	1·50	1·70	2·55	4·99	8·56	9·66

System B. Initial [C_6H_{11}·NCO] = 0·0700M.

(3) Initial [NH_2Ph] = 0·0698M.					
10^3[Carb. B] (M)	0·1	0·21	0·93	1·7	3·35
10^5k_o	0·17	0·24	0·45	0·65	0·95
(4) Initial [NH_2Ph] = 0·8375M.					
10^3[Carb. B] (M)	0·76	1·52	5·05	8·58	10·92
10^5k_o	0·71	0·87	1·21	1·65	2·02

found relationship in the alcohol–*iso*cyanate reaction suggests analysis of the results in terms of the following schemes of reaction mechanism:

For the true spontaneous reaction:

$$\left.\begin{array}{l} \text{Ar·NCO} + \text{NH}_2\text{R} \underset{k_5}{\overset{k_4}{\rightleftharpoons}} \text{Complex 1} \\ \text{Complex 1} + \text{NH}_2\text{R} \xrightarrow{k_6} \text{Ar·NH·CO·NHR} + \text{NH}_2\text{R} \end{array}\right\} \quad . \; . \; \text{(iii)}$$

whence, as in the alcohol reaction, stationary-state conditions give the relation

$$k_s = k_4k_6[\text{NH}_2\text{R}]/(k_5 + k_6[\text{NH}_2\text{R}]) \text{ or}$$
$$[\text{NH}_2\text{R}]/k_s = k_5/k_4k_6 + [\text{NH}_2\text{R}]/k_4 \; . \; . \; . \; . \; . \; . \; . \; . \; . \; . \; \text{(iv)}$$

For the product-catalysed reaction we then have:

$$\left.\begin{array}{l} \text{Ar·NCO} + \text{Ar·NH·CO·NHR} \underset{k_3}{\overset{k_1}{\rightleftharpoons}} \text{Complex 2} \\ \text{Complex 2} + \text{NH}_2\text{R} \xrightarrow{k_2} 2\text{Ar·NH·CO·NHR} \end{array}\right\} \quad . \; . \; . \; . \; . \; \text{(v)}$$

which gives the similar relation:

$$k_o - k_s = k_c'[\text{Carb.}] = k_1k_3[\text{Carb.}]/(k_2 + k_3[\text{NH}_2\text{R}]) \text{ or}$$
$$1/k_c' = k_2/k_1k_3 + [\text{NH}_2\text{R}]/k_1 \; . \; . \; . \; . \; . \; . \; . \; . \; . \; . \; \text{(vi)}$$

The values of k_s and k_c' for various initial concentrations of reactant amine, determined from the slopes and intercepts of the linear plots obtained for data exemplified in Table 5, are given, for two systems only, in Table 6. As required by the suggested mechanisms, a plot of [NH_2R]/k_s against [NH_2R] is linear (except for the value in parentheses), thus satisfying equation (iv), as also is the plot of $1/k_c'$ against [NH_2R], in accordance with equation (vi). From the slopes and intercepts of these plots the following approximate values of the various velocity coefficients are obtained:

	10^3k_1	k_2/k_3	10^5k_4	k_5/k_6
(*a*) 1·77 (±5%)	6·7 (±15%)	2·46 (±4%)	18 (±20%)
(*b*) 1·7 (±8%)	2·1 (±20%)	0·9 (±30%)	1·8 (±60%)

7 M

Confirmation of the self-consistency of the analysis was obtained by substituting the appropriate values of k_s and k_o' from Table 6 in equation (ii) (p. 4656) for each individual run in homogeneous solution. Linear plots were obtained in all cases for the whole course of each run, over the range of initial benzocaine concentrations 0·0335—0·5091M.

TABLE 6. *Variations of k_s and k_o' with initial* $[NH_2R]$ *in the reaction of* Ar·NCO–NH_2R.

(*a*) System A, initial [Ph·NCO] = 0·0710M: (*b*) System B, initial [C_6H_{11}·NCO] = 0·0700M.

(*a*) Initial $10^2[NH_2R]$ (M)	3·35	6·69	26·79	32·15	40·18	50·91
10^5k_s	1·05	1·20	2·15	2·00	2·15	2·85
$[NH_2R]/k_s$	3190	5575	12,470	16,080	18,690	(17,860)
$10^3k_o'$	10·7	6·51	4·01	3·92	3·43	2·60
$1/k_o'$	94	153	249	255	292	385
(*b*) Initial $10^2[NH_2R]$ (M)	6·982	55·84	83·75			
10^5k_s	0·15	0·40	0·65			
$[NH_2R]/k_s$	46,550	139,600	128,800			
$10^3k_o'$	2·89	1·87	1·24			
$1/k_o'$	346	568	808			

(Data for system B are restricted, but reveal the same general pattern.)

III(1). *Supersaturation Phenomena.*—The following results show that, even in the presence of undissolved product, the concentration of dissolved product still builds up to a supersaturated value. In runs in heterogeneous and in homogeneous media the constant values of heterogeneous k_o (k_o^s) and the instantaneous values of homogeneous k_o at the solubility concentrations of product (k_o^u), at very closely similar concentrations of reacting amine, are compared in Table 7. Although the values of $[NH_2R]$ in homogeneous media

TABLE 7. *Comparison of the values of k_o^s (heterogeneous systems) and k_o^u (homogeneous systems) at [Carb.] = solubility.*

Initially [Ar·NCO] = 0·07M.

System A

Heterogeneous			Homogeneous	
Mean $[NH_2·C_6H_4·CO_2Et]$ $(10^{-2}M)$	$10^5k_o^s$	Solubility [Carb. A] $(10^{-2}M)$	Mean $[NH_2·C_6H_4·CO_2Et]$ $(10^{-2}M)$	$10^5k_o^u$
47·29	12·8	2·42	48·49	9·2
38·43	11·1	2·00	38·18	9·0
29·50	9·67	1·59	30·56	8·3
24·66	8·26	1·36	25·43	7·6
11·05	6·07	0·72	12·67	4·5
5·47	5·06	0·46	6·23	4·2
2·10	4·89	0·30	3·05	4·2

System B

Mean $[NH_2Ph]$ $(10^{-2}M)$	$10^5k_o^s$	Solubility [Carb. B] $(10^{-2}$ mole $l.^{-1})$	Mean $[NH_2Ph]$ $(10^{-2}M)$	$10^5k_o^u$
106·4	2·59	1·03	—	—
79·8	2·11	0·784	82·97	1·62
51·28	1·68	0·580	55·26	1·44
24·60	1·35	0·421	—	—
4·95	1·04	0·317	6·66	1·08

are each slightly higher than are the corresponding values in the heterogeneous system, the differences are themselves too small to cause significant differences between k_o^u and k_o^s. Yet k_o^s is always ~20—40% greater than k_o^u. It follows that, even when undissolved solid is present, the concentration of dissolved product cannot immediately fall to its true solubility value. Careful examination of the instantaneous k_o values in initially homogeneous systems at, and immediately after, the first deposition of solid product, shows

that the value k_o^p at this point first continues to increase to k_o^m and then decreases to the equilibrium, constant value k_o^s, which, however, is always greater than k_o^u. This is illustrated by typical data for two systems in Table 8.

TABLE 8. *Increase in k_o in initially homogeneous systems after deposition of the urea product.*

System A.

(1) Initially: [Ph·NCO] = 0·0710M; [NH_2·C_6H_4·CO_2Et] = 0·3215M; [Carb. A] = 0.
Solubility [Carb. A] = 0·0163M: at deposition [Carb. A] = 0·0219M.

[NH_2·C_6H_4·CO_2Et] (M)	=	0·2996	0·2956	0·2887
10^5k_o	=	10·4 (k_o^p)	11·1 (k_o^m)	9·4

(2) Initially [Ph·NCO] = 0·0710M; [NH_2·C_6H_4·CO_2Et] = 0·2679M; [Carb. A] = 0.
Solubility [Carb. A] = 0·0136M: at deposition [Carb. A] = 0·0231M.

[NH_2·C_6H_4·CO_2Et] (M)	=	0·2448	0·2431	0·2265
10^5k_o	=	10·1 (k_o^p)	12·8 (k_o^m)	7·6

System B. Initially [C_6H_{11}·NCO] = 0·0700M.

No.	Initial [NH_2Ph] (M)	$10^5k_o^u$	$10^5k_o^p$	$10^5k_o^m$
1	0·06982	1·08	1·26	1·46
2	0·5584	1·44	1·94	2·11
3	0·8375	1·62	2·41	3·09

			[Carb. B] (10^{-3}M) to account for			[Carb. B] (10^{-3}M)	
			(*a*)	(*b*)	(*c*)	(*a*)	(*b*)
No.	$10^5(k_o^m - k_o^u)$	$10^5(k_o^m - k_o^p)$	solubility	k_o^m	$k_o^m - k_o^p$	formed $p \longrightarrow m$	deposited $p \longrightarrow m$
1	0·38	0·20	3·17	4·5	0·7	2·4	1·7
2	0·67	0·17	5·80	9·4	1·0	3·1	2·1
3	1·47	0·68	7·84	19·6	5·4	6·9	1·5

Thus the concentration of dissolved product to account for the value of k_o^m is greater than the true solubility value, and, during the period of the run between k_o^p and k_o^m, only a fraction of the new product formed has been deposited, the remainder further increasing the concentration of dissolved product notwithstanding the already supersaturated character of the medium. In harmony with this, similar small variations in the instantaneous values of k_o could sometimes be observed in *initially* heterogeneous runs for which the second-order plot is approximately linear (cf. Ib, p. 4656), the apparent " straight line " sometimes being a very shallow S-shaped curve. This is illustrated for system A in Table 9.

TABLE 9. *Small variations in k_o for the system A in the presence of excess of solid Carb. A.*

Initially [Ph·NCO] = 0·0739M; [NH_2·C_6H_4·CO_2Et] = 0·3110M.

[NH_2·C_6H_4·CO_2Et] (10^{-3}M)	Solubility [Carb. A] (10^{-3}M)	10^5k_o	[Carb. A] to account for k_o (10^{-3}M) *
30·55	1·67	8·2	1·58
29·92	1·63	9·35	1·86
29·29	1·61	10·4 (k_o^m)	2·14
28·75	1·58	9·95	2·01
28·29	1·56	8·7	1·70

* From runs in homogeneous media.

Except in the very early stages of reaction (line 1, Table 9) the concentration of dissolved product necessary to account for the observed value of k_o is always greater than the solubility value, even although an excess of undissolved solid is present throughout. Such phenomena are even more pronounced in System B in the presence of excess of solid Carb. B. Thus, (*a*) with initial concentrations [C_6H_{11}·NCO] = 0·0700M, [NH_2Ph] = 1·116M, the second-order plot is a shallow S-shaped curve (Figure, $C + D + E$); (*b*) with [C_6H_{11}·NCO] = 0·5593M, [NH_2Ph] = 0·5580M, the curve corresponds to type $D + E$; whilst (*c*) with

$[C_6H_{11}\cdot NCO] = 0{\cdot}0700$M, $[NH_2Ph] = 0{\cdot}2794$M, a straight-line plot (E only) is obtained, (cf. below).

III(2). *Interpretation of the Whole Reaction Course.*—The whole course of the S-shaped curve (see Figure) can now be interpreted. Depending on the value of r_t (and hence on the initial amine concentration), the effect of reactant amine concentration on the solubility of the product, and the value of r_d (supersaturation phenomena), the experimental results might (as they do) correspond to any portion of this total curve. In initially homogeneous medium increasing concentration in solution of the product causes a continuous rise in k_o (portion A). This continues into the supersaturated region until, at k_o^p, crystallisation begins (B). At this point $r_t > r_d$ and hence supersaturation increases, causing a further rise of k_o to its maximum value k_o^m (C). The increased distribution of crystal nuclei throughout the medium now greatly increases r_d, which becomes $> r_t$, the concentration of dissolved product falls, and so does the value of k_o (D) until, when equilibrium conditions $r_t = r_d$ are attained, the concentration of dissolved product remains approximately constant (but still higher than its true solubility value) and k_o^s remains constant for the remainder of the reaction, the second-order plot becoming linear (E).

In a very fast reaction, when r_t is very great, the consequent build up of supersaturation, and deposition of a large amount of solid urea, results in the attainment of the condition $r_d > r_t$ after only a short time interval, before initial readings are taken. Under these conditions, exemplified by case (b) (above), only sections $D + E$ of the curve are experimentally realised. Conversely, in a very slow reaction r_t is very small and never exceeds r_d: supersaturation conditions are never built up and $k_o^s = k_o^u$. Hence the second-order plot is linear (section E only) as exemplified by case (c) (above).

IV. *Reaction in Stirred Media.*—If this picture is essentially correct, efficient stirring of a heterogeneous reaction medium should greatly facilitate the attainment of the equilibrium $r_t = r_d$, in the medium already saturated with product and containing undissolved solid. Under such conditions the efficient distribution of crystal nuclei should reduce both the degree of supersaturation (and therefore the value of k_o) and the period during which $r_t > r_d$. Hence sections C and D of the curve should be telescoped into a very short time interval, and a good linear second-order plot should be obtained throughout the remainder of the run. Illustrative results are in Table 10. Experiments No. 29 and

TABLE 10. *Effect of stirring on the rate of the reaction* Ph·NCO–NH_2Ph (*System C*)

Initially: $[Ph\cdot NCO] = 0{\cdot}07$M; $[NH_2Ph] = 0{\cdot}175$M.

No.	Conditions *	Time of commencement of rapid deposition (min.)	Instantaneous 10^3k_o at 15 min.
25	0·0231 g.; n.s.	10	1·80
29	0·0696 g.; s.	3	1·38
30	0·6611 g.; s.	3	1·41
31	0·0631 g.; r.s.	2·5	1·24

* Wt. of added Carb. C; n.s. = no stirring; s. = stirring; r.s. = rapid stirring.

30 show that, with stirring, a 10-fold variation in the amount of solid urea present has no effect on the rate, confirming the absence of surface catalysis or absorption phenomena. The expected fall in k_o due to rapid stirring is realised. A similar effect is produced when very large amounts of solid are added (Table 3), the small reduction in the k_o^s value arising from the increased availability of solid nuclei. The explanation suggested for the variation in k_o is the only one which satisfactorily accounts for all the experimental observations.

V. *Reaction Mechanism and the Function of Catalysts.*—Although the experimental results are satisfactorily represented by the relation, $k_o = k_s + k_c'[\text{Carb.}]$, yet $k_s = f[NH_2R]$ and $k_c' = f(1/[NH_2R])$, and hence any numerical values of k_s and k_c' are valid at only the one particular concentration of reactant amine. Explicit formulation of the *catalytic*

function of reactant amine (eqn. iii) and product (eqn. v) is not possible for several reasons. First, it is not possible to vary the amine or product independently of one another. Secondly, since both mechanisms (iii) and (v) involve the reversible formation of different intermediate complexes, coupling of the two mechanisms through the reverse dissociation of these two complexes is possible, *i.e.*, they cannot, with certainty, be regarded as isolated, simultaneous paths for the formation of the product. No account of any association phenomena (Part VI) is possible. In spite of these limitations certain tentative deductions regarding the general nature of the catalytic action may be drawn.

(1) *The true "spontaneous" reaction.* The effect of varying (1) the amine and (2) the *iso*cyanate on the values of k_s obtained under constant amine and *iso*cyanate concentrations (both ~0·07M) is as follows: (*a*) with phenyl *iso*cyanate the values are $10^5k_s = 1{\cdot}20$ and 14·4 for benzocaine and aniline respectively; (*b*) with aniline, $10^5k_s = 14{\cdot}4$, 12·6, and 0·15 for its reaction with phenyl, *p*-methoxyphenyl, and *cyclo*hexyl *iso*cyanate, respectively. The efficiency of the two bases thus runs parallel with their basic strengths and, for aniline, the velocity of the spontaneous reaction with Ar·NCO decreases in the order Ar = Ph > *p*-MeO·C_6H_4 ≫ *cyclo*-C_6H_{11}, as was found for the corresponding reactions with alcohols.[4a] It is therefore probable that both amine and alcohol reactions involve closely similar mechanisms and hence the former also involves a nucleophilic attack of the amine at the carbonyl group of the *iso*cyanate: $\overset{\curvearrowright}{NH_2R}\ C(:NH)\overset{\curvearrowright}{=}O$. The kinetic results can give no explanation *why* further attack by a second amine molecule is necessary to complete the proton transfer, but several schemes can be envisaged.

(2) *The product-catalysed reaction.* The presence both of basic tervalent nitrogen centres and of acidic hydrogen, in the groups $H{-}\overset{|}{N}{-}\overset{|}{C}{=}O$ present in the urea products, makes it theoretically possible for them to function as either acid or base catalysts. Results obtained for the tertiary-base-catalysed reaction (following paper) show that, for constant concentrations of *cyclo*hexyl *iso*cyanate and aniline (both ~0·07M) the values of $10^3k_c'$ for triethylamine and for the product Ph·NH·CO·NH·C_6H_{11} are 0·249 and 2·89 respectively, *i.e.*, the catalytic coefficient of the very much weaker product-base is ~11 times greater than that of the strong base triethylamine. This suggests that the product is functioning as an acid catalyst, rather than as a base, facilitating the reaction by association of the acidic hydrogen with the carbonyl-oxygen atom, and thus increasing the requisite polarisation of the carbonyl group towards nucleophilic attack by the reactant amine, as in the formula $ArN{=}\overset{\delta+}{C}{=}\overset{\curvearrowright}{O}\rightarrow HN(Ar)\cdot CO\cdot NHR$. The observed acid catalysis by organic acids on the amine–*iso*cyanate reaction [2,3] and on the phenol–*iso*cyanate reaction [6] probably functions by a similar mechanism. This acid-catalysed mechanism for the urea product does not, of course, exclude the possibility that the product might also function as a weak base catalyst in a manner similar to that postulated for the reactant amine.

Experimental

Materials.—Rigid precautions were taken to remove all traces of moisture from materials used and for their storage under completely anhydrous conditions.

Benzene.—"AnalaR" benzene was repeatedly refluxed over phosphoric oxide and fractionated through a good column. The fraction of constant b. p. was then repeatedly refluxed over fresh sodium wire and again fractionated. The sample, b. p. 79·7°/756 mm., was stored over sodium wire in a carefully dried vessel, fresh sodium being added from time to time. No carbanilide formation was observed after long storage of dry phenyl *iso*cyanate in this solvent.

Aniline.—"AnalaR" aniline was refluxed under reduced pressure over anhydrous potassium carbonate and was then kept sealed in contact with fresh amounts of this drying agent for several weeks. The middle fraction, obtained by careful fractionation through a good column, was repeatedly treated with 10 wt. % of powdered potassium hydroxide, refluxed for 1 hr. at

[6] Tarbell, Mallatt, and Wilson, *J. Amer. Chem. Soc.*, 1942, **64**, 2229.

200° over this drying agent, and then repeatedly fractionated (column) under reduced pressure. The sample, b. p. 86°/25·5 mm., was sealed in dry vessels. Samples were redistilled under reduced pressure immediately before use. Complete absence of moisture in the aniline was proved by the reproduction of various kinetic runs with aniline which had previously reacted with ~20 wt. % of dry phenyl *iso*cyanate: the unchanged aniline, recovered by fractionation under reduced pressure, had b. p. 71°/14 mm. In typical duplicate experiments the steady $10^5k_0^s$ values, (*a*) before *iso*cyanate treatment and (*b*) after such treatment, were: (1) (*a*) 90·5, (*b*) 88·8; (2) (*a*) 63·4, (*b*) 64·8.

iso*Cyanates*.—These were pure samples used in previous work.[4] They were repeatedly fractionated over phosphoric oxide and were again distilled from phosphoric oxide immediately before use: phenyl, b. p. 54°/15·5 mm.; *p*-methoxyphenyl, b. p. 113°/23 mm.; and *cyclo*hexyl *iso*cyanate, b. p. 59°/17 mm.

NN'-*Disubstituted Ureas*.—These were prepared from the appropriate amine and *iso*cyanate, recrystallised from an appropriate dry solvent to constant m. p., and stored over phosphoric oxide in a vacuum. Physical and analytical data are recorded in Part VI.

Apparatus.—All-glass apparatus, other than volumetric, was stored in an electric oven at 110° and then in a vacuum over phosphoric oxide before use. Pyrex reaction vessels were ignited just short of red heat and cooled in a vacuum over phosphoric oxide. Calibrated standard flasks and pipettes were washed only with dry solvents, dried in a current of dry air, and stored over phosphoric oxide in appropriate cylindrical desiccators immersed in the thermostat, which was of standard type maintained at 20° ± 0·005°.

Velocity Determinations.—Reaction vessels (except for stirred experiments) were of the pattern used previously.[4a] Because of the separation of solid product, samples were removed by pipettes to the ends of which were attached sintered-glass filter-sticks, suction being applied through a drying train. Unchanged *iso*cyanate was determined by the micro-adaptation of Stafford and Stagg's method, described in previous papers in this series.[4] Calibration curves, prepared for each *iso*cyanate, from concentrations 0 ⟶ 0·07M, were accurate straight lines passing through the origin; determined values corresponded to 100% ± 0·2% (0·07M region) to 100% ± 0·8% (0·02M-region) of the actual weight of *iso*cyanate present. Calibration curves were checked at intervals during the investigation, and each time a fresh sample of *iso*cyanate was employed.

In stirred experiments the modified reaction vessel consisted of a two-necked ground-joint flask fitted with a mercury-sealed stirrer. Reaction was started by final additions of the *iso*cyanate solution (at temperature equilibrium with the thermostat) through the side-neck, which was also used for withdrawal of samples.

The number of individual runs (each involving 10—15 determinations of k_0) was so large that recording of individual results is impracticable and summaries of the data are recorded in the various Tables.

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[*Received, May 31st,* 1957.]

936. *The Mechanism of the Reaction of Aryl* iso*Cyanates with Alcohols and Amines. Part VIII.*[1] *The Base-catalysed Reaction with Amines.*

By JOHN W. BAKER and D. N. BAILEY.

Kinetic examination of the reaction

$$Ar{\cdot}NCO + NH_2R \longrightarrow Ar{\cdot}NH{\cdot}CO{\cdot}NHR$$

for various reactant pairs, in the presence of triethylamine and other tertiary amines (B) in dry benzene at 20° reveals that, superimposed upon the true spontaneous and product-catalysed reactions, are (1) a base-catalysed reaction, $Ar{\cdot}NCO + B \rightleftharpoons$ Complex; Complex $+ NH_2R \longrightarrow Ar{\cdot}NH{\cdot}CO{\cdot}NHR + B$, and (2) a combined product–base–catalysed reaction involving mutual action by these two catalytic entities, possibly: $Ar{\cdot}NCO + B + Ar{\cdot}NH{\cdot}CO{\cdot}NHR \rightleftharpoons$ ternary complex; ternary complex $+ NH_2R \longrightarrow 2Ar{\cdot}NH{\cdot}CO{\cdot}NHR + B$. With $B = NEt_3$, the reaction velocity increases in the order Ar = C_6H_{11} (*cyclo*hexyl) $\ll$ *p*-MeO·C_6H_4 < Ph, *i.e.*, with increasing conjugation (*a*) of the nitrogen atom with Ar, Ar—N=C=O, which, competing with the conjugation (*b*), renders the carbonyl group more susceptible to nucleophilic attack. In agreement with this, for Ar = Ph, the catalytic effect is greater, the greater is the basic strength (nucleophilic power) of B, *i.e.*, $B = NEt_3$ ($K_b = 5{\cdot}46 \times 10^{-4}$) > C_5H_5N ($K_b = 2{\cdot}3 \times 10^{-9}$), but, as in the alcohol reaction, the much weaker catalytic effect of $C_6H_5{\cdot}NMe_2$ ($K_b = 1 \times 10^{-9}$) is anomalous, owing to sterically hindered attack.

LIKE the *iso*cyanate–alcohol reaction,[2a] the corresponding *iso*cyanate–amine reaction $Ar{\cdot}NCO + NH_2R \longrightarrow Ar{\cdot}NH{\cdot}CO{\cdot}NHR$ is catalysed by tertiary amines.* The similar mechanisms already established for the spontaneous and base-catalysed alcohol reaction,[2] and for the spontaneous and product-catalysed amine reaction,[1] strongly suggest a mechanism ($B = NR_3$):

$$Ar{\cdot}NCO + B \underset{k_s}{\overset{k_7}{\rightleftharpoons}} \text{Complex; Complex} + NH_2R \xrightarrow{k_9} Ar{\cdot}NH{\cdot}CO{\cdot}NHR + B \quad . \quad \text{(i)}$$

as probable for the base-catalysed reaction with amines. Superimposition of such a base-catalysed reaction upon the spontaneous (k_s) and product-catalysed reactions (preceding paper) would require the experimental, second-order velocity coefficient k_e to be represented by the expression:

$$k_e = k_s + k_c'[\text{Carb.}] + k_c[B] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(ii)}$$

where k_s and k_c' are functions of amine concentration.[1] Application of stationary state conditions gives the relation:

$$k_{bi} = k_c[B] = k_e - (k_s + k_c'[\text{Carb.}]) = k_7k_9[B]/(k_8 + k_9[NH_2R]) \quad . \quad \text{(iii)}$$

i.e., the linear relation,

$$1/k_c = [B]/k_{bi} = k_8/k_7k_9 + [NH_2R]/k_7 \quad . \quad . \quad . \quad . \quad . \quad \text{(iv)}$$

* To avoid confusion the term " base " (B) is used throughout for the tertiary-amine catalyst, and " amine " for the reactant amine NH_2R. The various *k* values are denoted by subscripts which differentiate them from those used for the *k* values of concomitant reactions, described in Part VII.

[1] Part VII, preceding paper.
[2] Baker and Gaunt, *J.*, 1949, (*a*) 9, (*b*) 19, (*c*) 27.

where k_{bl} = the apparent second-order velocity coefficient for the isolated base-catalysed reaction.

The relations (iii) and (iv) can only be tested by the determination, at identical values of amine and urea concentration, of k_e in the presence of an added tertiary base, and of $k_s + k'$[Carb.] in the absence of the base. The second-order plots obtained in the presence of a base exhibit the same characteristics as those revealed in the spontaneous reaction (Part VII, Figure), the particular portions of this curve followed by the reaction depending on the initial concentration of the urea, on its solubility, and on the reaction rate.

System A * (Ph·NCO–*p*-NH_2·C_6H_4·CO_2Et) was first examined with constant initial [Ph·NCO] (0·0726M) and [NH_2R] (0·1292M) in initially homogeneous media (*i.e.* initial [Carb. A] = 0) but with varying concentrations of triethylamine as the base catalyst, in dry benzene solution at 20°. The second-order plots of all such runs were shallow S-shaped curves in which k_e first increases as [Carb. A] increases until, after deposition of solid product, it then decreases. In all cases, however, the [Carb. A] builds up to 2—4 times its saturation value before crystallisation begins, *e.g.*:

[NEt_3] (10^{-3}M)	3·0	5·0	7·5	9·9	14·9	19·8	24·8	29·8
[Carb. A] at deposition (10^{-3}M)	20	18	28	14	24	26	27	28
Saturation [Carb. A] † (10^{-3}M) †	6·85	6·95	6·50	7·10	6·70	6·60	6·60	6·65

† At deposition: from data in Part VI (p. 4650).

The irregular nature of the commencement of product deposition from initially homogeneous media is again evident.

From these experiments (see p. 4668), plots (P1) of the instantaneous k_e values (as ordinates) against corresponding values of [Carb. A] (determined by either tangent or small interval methods) were made at different base concentrations, including the case when [NEt_3] = 0. These plots are all accurately linear, but the slope of the lines, *i.e.*, the apparent k_e' value, increases as [NEt_3] increases. From these graphs a second series of plots (P2) of k_e against [NEt_3] at constant [NH_2R] and constant [Carb. A] were made. The relevant data are in Table 1. These plots (P2) are again accurately linear, the slope

TABLE 1. *Values of* 10^5k_e *at constant* [NH_2R] *and* [*Carb. A*] *values for various values of* [NEt_3] *for system A.*

No.	1	2	3	4	5	6	7	8
[Carb. A] (10^{-3}M)	0	0·5	0·7	1·0	1·5	2·0	2·5	3·0
[NH_2R] (10^{-3}M) ...	12·92	12·42	12·22	11·92	11·42	10·92	10·42	9·92
[NEt_3] (10^{-3}M)	10^5k_e							
0	2·00	3·90	4·50	5·50	7·20	9·00	10·8	12·4
0·298	12·6	14·9	15·8	17·1	19·7	21·9	24·2	26·5
0·496	16·1	19·0	20·1	22·0	25·0	28·0	31·1	34·0
0·745	25·7	29·0	30·2	32·2	35·8	39·1	42·6	46·0
0·992	27·0	33·2	35·8	39·6	45·9	52·1	58·3	64·7
1·498	45·9	51·1	53·3	56·7	62·2	67·9	73·3	78·9
1·985	59·6	65·1	67·6	71·0	76·6	82·3	88·0	93·7
2·48	73·5	81·0	84·0	88·8	96·4	104	111	119
2·98	95·0	103	107	112	121	129	138	147

of the lines increasing from No. 1 to 8, *i.e.*, the apparent k_e value increases as [Carb. A] increases and [NH_2R] decreases. This observed dependence of k_e on [Carb. A] or, alternatively, of k_e' on [NEt_3] is not accounted for by the mere superimposition of mechanism (i) alone (to give ii), and the inadequacy of this treatment is further revealed by the fact that the plot of $1/k_e$ against [NH_2R], although linear as required by equation

* For key, see Part VII, preceding paper.

(iv), cuts the $1/k_e$ axis at a negative value when $[NH_2R] = 0$. This would require the impossible condition that k_8/k_7k_9 (equation iv) should have a negative value.

The increase in the apparent k_c' values with increase in $[NEt_3]$ means that the total effect of the urea and base catalysts, acting conjointly, is greater than the sum of their separate actions. This indicates a superimposed mechanism which involves both catalytic entities. Since previous evidence has suggested that the urea probably functions as an *acid* catalyst, the combined acid-catalysis by the product and base-catalysis by triethylamine could be envisaged as $Et_3N{\rightarrow}C(:NAr){=}O{\rightarrow}HN(Ar){\cdot}CO{\cdot}NHR$, which is represented by

$$Ar{\cdot}NCO + Ar{\cdot}NH{\cdot}CO{\cdot}NHR + NEt_3 \underset{k_{11}}{\overset{k_{10}}{\rightleftharpoons}} \text{ternary complex } *$$

$$\text{ternary Complex} + NH_2R \xrightarrow{k_{12}} 2Ar{\cdot}NH{\cdot}CO{\cdot}NHR + NEt_3$$

The new catalytic coefficient k_c'' would then be determined by the relation, $k_c''[ArNCO][NEt_3] = k_{10}k_{12}[\text{Carb. A}][NEt_3]/(k_{11} + k_{12}[NH_2R])$. The experimental value of the composite second-order velocity coefficient k_e for the total base-catalysed reaction would then be represented by the sum:

$$k_e = k_s + k_c'[\text{Carb.}] + k_c[B] + k_c''[\text{Carb.}][B] \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(v)}$$

The data available permit an approximate test of this mechanism, since it requires that:

$$k_c''[\text{Carb.}][B] = k_e - (k_s + k_s'[\text{Carb.}] + k_c[B]) = K \quad . \quad . \quad . \quad \text{(vi)}$$

Hence, at constant [Carb.], $K/[B]$ is a constant. This may be tested from the data available from plot P1. The values of k_e at [Carb.] = 0·020M were read off for various values of $[NEt_3]$; $k_s + k_c[B]$ values are given by the intercepts on the k_e axis ([Carb. A] = 0); and $k_c'[\text{Carb.}]$ from the plot when $[NEt_3] = 0$. The relevant results are in Table 2.

TABLE 2. *Values of K/[B] for System A with triethylamine catalysis in dry benzene at 20° when [Carb. A] = 0·020M and [NEt_3] is varied.* (K *in mole*$^{-1}$ *l. sec.*$^{-1}$.)

$[NEt_3]$ (10^{-3}M)	2·98	4·96	7·45	9·92	14·98	19·85	24·8	29·8
10^4K	2·5	5·0	6·5	18	15	15·5	23·5	27·5
$10^4K/10^3[NEt_3]$	0·84	1·00	0·97	(1·80)	1·00	0·78	0·95	0·92

If the value in parentheses is neglected, the values of $K/[NEt_3]$ show a random variation around a constant value 0·92 ± 0·07, as required by (vi). In view of the approximations essential to this complicated analysis the agreement with the requirements of the composite mechanism (v) is regarded as satisfactory. It follows from this that the true base-catalytic coefficient k_c can be determined only at [Carb. A] = 0, *i.e.*, from the slope of the linear plot No. 1 of P2 (Table 1), in which k_e is plotted against $[NEt_3]$ at constant $[NH_2{\cdot}C_6H_4{\cdot}CO_2Et]$ and [Carb. A] = 0.

The validity of mechanism (i) and its derived relation (iv) for the isolated base-catalysed reaction was tested (for System A) by examination of the effect of variation in the initial $[NH_2R]$ from 0·0646 to 0·3877M when the initial concentrations of phenyl *iso*cyanate (0·0710M) and triethylamine (0·0121M) were maintained constant, in homogeneous media (initially [Carb. A] = 0). From the second-order plots, the varying values of k_e at increasing concentrations of [Carb. A] were determined as the reaction progressed. Plots (P3) of k_e against [Carb. A] are accurately linear, and from these the values of k_e at

* The formation of such a ternary complex might, of course, involve successive equilibria between the *iso*cyanate and one catalytic entity to give a 1 : 1 complex, and between this 1 : 1 complex and the second catalytic entity to give a 1 : 2 complex.

[Carb. A] = 0 were determined. The relevant data are in Table 3, the values of k_e and its reciprocal thus obtained being independent of any interaction which occurs between triethylamine and product catalysis. With increasing [NH_2·C_6H_4·CO_2Et], k_o increases, but both k_e and k_{bi} decrease as required by equation (iii), and the plot of $1/k_e$ against

TABLE 3. *Variation of k_o with* [NH_2R] *in dry benzene at* 20° (R = C_6H_4·CO_2Et)

Initially: [Ph·NCO] = 0·0710M; [Carb. A] = 0; [NEt_3] = 0·0121M.

No.	Initial [NH_2R] (10^{-2}M)	10^5k_o *	10^5k_e	$10^5k_{bi} = 10^5k_e$ [NEt_3]	10^2k_e	$1/k_e$
85	6·46	1·2	43·0	41·8	3·45	28·9
86	12·92	1·5	41·5	40·0	3·30	30·2
87	25·85	1·9	40·9	39·0	3·22	31·0
88	31·02	2·1	40·2	38·1	3·14	31·7
89	38·77	2·5	39·7	37·2	3·07	32·5

* $k_o = k_s + k_c'$ [Carb.]; since [Carb. A] = 0, $k_o = k_s$.

[NH_2·C_6H_4·CO_2Et] is linear, thus satisfying the derived relation (iv). Thus the values $k_7 = 0·089$ and $k_9/k_8 = 0·04$ are derived.

In heterogeneous media, *i.e.*, those initially saturated with Carb. A, supersaturation phenomena make reproducibility of conditions more difficult, and the steady values of k_e (*i.e.*, those when the second-order plots have become linear), although showing a general trend towards decreasing as the initial [NH_2·C_6H_4·CO_2Et] increases, are somewhat erratic, as shown in Table 4. In order to smooth out these experimental errors the smoothed plots

TABLE 4. *Variation of k_o with varying initial* [NH_2R] *for the base-catalysed system A in heterogeneous media initially saturated with Carb. A* (R = C_6H_4·CO_2Et).

Initially: [Ph·NCO] = 0·0708M; [NEt_3] = 0·0120M throughout.

No.:	90	91	92	93	94	95	96
Initial [NH_2R] (10^{-2}M)	46·61	38·83	31·10	25·92	12·96	6·48	3·24
Saturation [Carb. A] (10^{-2}M)	2·46	2·07	1·70	1·44	0·80	0·48	0·32
10^5k_e	44·8	46·2	44·2	48·2	46·1	49·6	56·1

TABLE 5. *Smoothed values of k_e at various* [NH_2R] *in System A in heterogeneous media* (R = C_6H_4·CO_2Et).

[NH_2R] (10^{-2}M)	10^5k_e	10^5k_o	10^5k_{bi}	10^2k_e	$1/k_e$	[NH_2R] (10^{-2}M)	10^5k_e	10^5k_o	10^5k_{bi}	10^2k_e	$1/k_e$
5	52·0	4·7	47·3	4·63	21·5	30	46·2	9·3	36·9	3·61	27·6
10	48·7	5·5	43·2	4·23	23·6	40	44·9	11·1	33·8	3·31	30·1
20	47·5	7·5	40·0	3·92	25·5	50	43·6	13·0	30·6	3·00	33·3
25	46·8	8·4	38·4	3·76	26·5						

of k_e and k_o against initial [NH_2·C_6H_4·CO_2Et] were subtracted to give the plot of $k_{bi}(= k_e - k_o)$ against [NH_2·C_6H_4·CO_2Et]. The derived values are given in Table 5.

Despite the fact that, in these systems, k''[Carb. A][B] is not zero, behaviour parallel to that shown in homogeneous media is observed, *i.e.*, (*a*) k_{bi} decreases as [NH_2R] increases as required by equation (iii), and (*b*) the plot of $1/k_e$ against [NH_2R] is linear (equation iv) as is required by mechanism (i). These results thus confirm the conclusions reached in the study in homogeneous media.

System C.—Owing to the greater speed of this reaction and the greater insolubility of the product, this system cannot be examined under homogeneous conditions, but a more limited series of experiments in media saturated with Carb. C revealed the same general pattern, the initial high value of k_e decreasing to a value which then remained constant over a large percentage of the total reaction. The essential data are summarised in Table 6.

Effect of Varying the iso*Cyanate Component.*—Limited examination of systems B and D was made, chiefly in order to determine the effect of varying the nature of the *iso*cyanate on the velocity of the triethylamine-catalysed reaction with aniline. In system B, k_e

initially increases and then decreases to a constant value, whilst in system D the initial high rates rapidly decrease to give a k_e value which remains constant over ~30—80% of the reaction course.

In triethylamine-catalysed systems of initial concentrations [Ar·NCO] = [NH_2Ph] = 0·07M, all saturated with respect of the products, the corresponding values of k_e and k_c are in Table 7. Thus, in base-catalysed systems, both k_e and the apparent k_c increase in the

TABLE 6. *Triethylamine-catalysed reaction of system C initially saturated with Carb. C, in dry benzene at* 20°.

Initially: [Ph·NCO] = [NH_2Ph] = 0·0698M.

No.	[NEt_3] (10^{-3}M)	Initial 10^5k_e	Mean steady 10^5k_e	Percentage reaction †
72	0	78·5	55·1 ± 0·6 (3) *	31·9—50·7
73	0·741	128	82·0 ± 1·5 (7)	22·6—63·5
74	1·48	127	113 ± 3 (8)	24·2—75·8
75	2·37	177	153 ± 5 (6)	47·2—77·8
76	2·97	211	183 ± 6 (6)	34·7—81·5
77	4·15	274	245 ± 4 (6)	40·8—85·4
78	5·94	369	331 ± 7 (5)	31·7—81·4

* Number of separate observations in parentheses.
† Over which a steady k_e value was observed.

TABLE 7. *Values of* k_e *and* k_c *for the triethylamine-catalysed systems* Ar·NCO–NH_2Ph.

	[NEt_3] (10^{-3}M)	0	3	6		[NEt_3] (10^{-3}M)	0	3	6
Steady 10^5k_e	Ar = Ph	58·4	169	314	10^3k_c	Ar = Ph	—	372	430
	Ar = *p*-MeO·C_6H_4	69·2	125	194		Ar = *p*-MeO·C_6H_4	—	192	212
	Ar = C_6H_{11}	1·04	1·11	1·20		Ar = C_6H_{11}	—	0·227	0·270

order Ar = $C_6H_{11} \ll$ *p*-MeO·C_6H_4 < Ph. This is in agreement with the postulated nucleophilic attack of amine and catalyst base on the polarised carbonyl group of the *iso*cyanate, the competing conjugation of the nitrogen with the carbonyl group Ar—N=C=O being at a maximum when all conjugation with the group Ar is eliminated in the *cyclo*hexyl compound, and the order is identical with that previously established [3] for the alcohol reaction.

Variation of the Tertiary Base Catalyst.—System C was also examined with pyridine and dimethylaniline severally as the base catalysts. The results are summarised in Table 8, and should be compared with those for triethylamine in Table 7.

TABLE 8. *Values of steady* k_e *in System C catalysed by* NR_3 = (a) *pyridine, and* (b) *dimethylaniline in dry benzene at* 20°.

Initially: [Ph·NCO] = [NH_2Ph] = 0·070M.

No.	[NR_3] (10^{-3}M)	10^5k_e	10^3k_e	No.	[NR_3] (10^{-3}M)	10^5k_e	10^3k_e
—	0	58·4	—	(*b*) 105	5·919	58·8	10·4
(*a*) 102	3·061	82·3	77·8	106	11·84	70·9	
103	6·116	109		107	23·65	76·3	
104	12·24	149					

The stronger base triethylamine ($K_b = 5·65 \times 10^{-4}$) is a much more effective catalyst than is the weaker pyridine ($K_b = 2·3 \times 10^{-9}$), and the anomalous, very weak catalytic effect of the almost equally strong base dimethylaniline ($K_b = 1 \times 10^{-9}$), observed in the alcohol reaction and attributed to sterically hindered attack,[3, 2b] is again marked, although, in the amine reaction, a weak catalytic effect is detectable at high concentrations of this catalyst.

[3] Baker and Holdsworth, *J.*, 1947, 713.

XUM

The composite mechanism (v) is the only one which satisfactorily accounts for the *iso*cyanate–amine reaction in the presence of a tertiary base catalyst. Each of the separate routes to the formation of the urea, however, reveals the same characteristic pattern previously established for the alcohol reaction, and is of the general form involving attack by an amine or alcohol molecule on a reversibly formed 1 : 1 or 1 : 2 complex between the *iso*cyanate and a catalytic entity, which may be the reactant amine or alcohol itself, the product, or an added tertiary base. There is thus a unified pattern throughout the whole of the reactions of aryl *iso*cyanates with nucleophilic reagents, but kinetic analysis is unable to provide information as to why the attack of a second molecule of the reactant seems to be essential to complete the proton-transfer to give the final product when the reactant itself is the catalyst.

Experimental

The preparation and purification of the materials used, and the experimental techniques were identical with those described in Part VII and in previous papers in this series. The tertiary bases were dried by long contact with potassium hydroxide. After careful fractionation, the fraction of constant boiling point was refluxed over freshly ignited calcium oxide, and again fractionated through an efficient column, giving: triethylamine, b. p. 89°; pyridine, b. p. 113°/752 mm.; dimethylaniline, b. p. 76°/15 mm. They were stored over potassium hydroxide and redistilled immediately before use.

The number of experiments is too large to permit individual record; analyses of the results are recorded in the various Tables. As an illustration, the experimental data for the system phenyl *iso*cyanate–benzocaine (system A) with triethylamine catalysis in dry benzene at 20°, from which the plots P1 (p. 4664) were obtained, are recorded.

Values of instantaneous k_e from the experimental second-order plots in a homogeneous system initially 0·0726M *in* Ph·NCO *and* 0·1292M *in benzocaine, for varying concentrations of triethylamine, up to the point* (*) *when deposition of product commenced. Concentrations are in mole* $l.^{-1}$.

No.	10^2[NEt_3]	10^2[Carb. A]	10^2[$NH_2{\cdot}C_6H_4{\cdot}CO_2Et$]	10^5k_e
64	0·003	0·63	12·29	15·3
	,,	1·30	11·62	18·3
	,,	2·01 *	10·91	20·6
	,,	—	10·32	20·6
65	0·005	0·58	12·34	19·6
	,,	1·21	11·71	23·3
	,,	1·76 *	11·16	25·8
	,,	—	10·49	27·0
66	0·0075	0·63	12·29	30·6
	,,	1·23	11·69	33·5
	,,	1·76	11·16	35·6
	,,	2·27	10·65	41·1
	,,	2·81 *	10·11	44·8
	,,	—	9·65	46·8
67	0·010	0·33	12·59	30·5
	,,	0·84	12·08	37·9
	,,	1·38 *	11·54	44·0
	,,	—	11·03	46·6
68	0·015	0·50	12·42	49·2
	,,	0·96	11·96	57·8
	,,	1·51	11·41	63·7
	,,	2·01	10·91	66·1
	,,	2·43 *	10·49	73·5
	,,	—	9·65	58·4
69	0·0199	0·92	12·00	69·7
	,,	1·26	11·66	74·0
	,,	1·89	11·03	78·0
	,,	2·26	10·66	84·0
	,,	2·64 *	10·28	90·1
70	0·0248	0·46	12·46	80·0
	,,	0·79	12·13	84·9
	,,	1·17	11·75	95·5
	,,	1·68	11·24	99·5
	,,	2·22	10·70	106
	,,	—*	9·77	90·3
71	0·0298	0·58	12·34	105
	,,	1·05	11·87	111
	,,	1·55	11·37	122
	,,	2·01	10·91	130
	,,	2·43	10·49	135
	,,	—*	9·69	115

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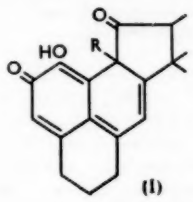
[*Received, May 31st,* 1957.]

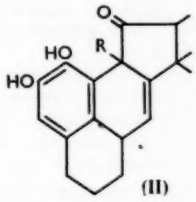
937. *Pristimerin. Part II.*[1] *Further Reactions involving the Chromophore.*

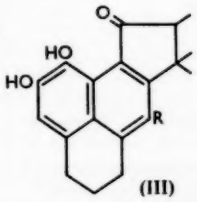
By P. K. Grant and A. W. Johnson.

Methylation of pristimerin by dimethyl sulphate, potassium carbonate, and acetone is shown to involve an addition of acetone to the pristimerin chromophore, a reaction which is catalysed by acid as well as by alkali. The product of addition of hydrogen chloride to pristimerin is also formulated.

In an earlier paper,[1] it was suggested that the wood pigment pristimerin, $C_{30}H_{40}O_4$, isolated from *Celastrus dispermus* and *Denhamia pittosporoides* (Celastraceae), contained the partial structure (I; R = OMe or Me), and that the related compound, celastrol, contained the unit (I; R = OH or Me). On the basis of structure (I), we formulated dihydropristimerin (pristimerol) as (II; R = OMe or Me), a rearrangement product obtained by the action of hot dilute sulphuric acid on pristimerin, as (III; R = OMe or Me), and the Thiele acetylation product as (IV; R = OMe or Me).


(I)


(II)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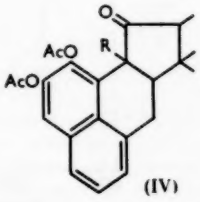

(IV)

Shah, Kulkarni, and Thakore [2] prepared " methylated pristimerin," $C_{30}H_{42}O_4$, by using dimethyl sulphate in acetone in presence of potassium carbonate. They recognised that the product was benzenoid from its ultraviolet absorption spectrum, that it also contained an aliphatic double bond (perbenzoic titration; positive tetranitromethane test), and that it formed a 2 : 4-dinitrophenylhydrazone by a condensation assumed to involve the original inert carbonyl group of pristimerin. Reduction of the methylated product by lithium aluminium hydride gave a secondary alcohol, which was also assumed to be derived from the inert keto-group. Re-examination of this compound has led us to amend the molecular formula to $C_{35}H_{50}O_5$ although we agree with the Indian workers that it contains three methoxy-groups, a benzene ring, and an isolated double bond. The additional oxygen atom is contained in an aliphatic ketone group (band in infrared spectrum at 1713 cm.$^{-1}$), and the inert carbonyl group of pristimerin (band at 1724 or 1718 cm.$^{-1}$ in chloroform solution) is retained. The 2 : 4-dinitrophenylhydrazone, $C_{41}H_{54}O_8N_4$, which is yellow, still shows the band (1718 cm.$^{-1}$ in chloroform) corresponding to the inert carbonyl group in the infrared spectrum, and the visible and ultraviolet absorption spectrum corresponds to a derivative of a saturated ketone. The reaction is therefore interpreted as the addition of acetone across the activated methylene-quinone system of pristimerin to give structure (V; R = OMe or Me, R′ = H), an acetonylpristimerol which is converted by dimethyl sulphate into the corresponding dimethyl ether (V; R = OMe or Me, R′ = Me).

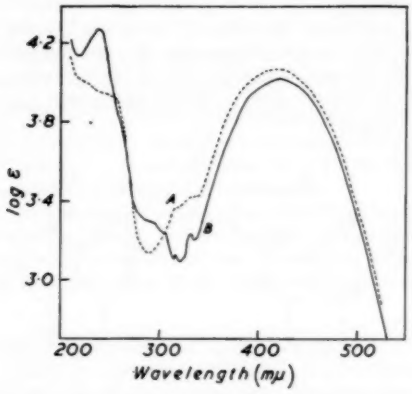
The view expressed by the Indian workers that the active ketonic group of (V; R = OMe or Me, R′ = Me) corresponds to the inert ketone of pristimerin is therefore erroneous and is attributable to their use of an incorrect molecular formula. The alcohol formed by reduction of the derivative (V; R = OMe or Me, R′ = Me) should be formulated as $C_{35}H_{52}O_5$ rather than $C_{30}H_{44}O_4$,[2] and is produced by reduction of the acetonyl group.

[1] Part I, Grant and Johnson, *J.*, 1957, 4079.
[2] Shah, Kulkarni, and Thakore, *J.*, 1955, 2515.

XUM

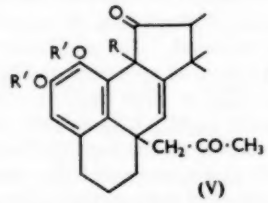
Examples of the direct addition of acetone to an unsaturated system are not common [3] and the high yield of adduct obtained in the present instance is evidence of the pronounced reactivity of the methylene-quinone system in pristimerin.

The dihydroxy-compound (V; R = OMe or Me, R′ = H), $C_{33}H_{46}O_5$, was obtained by the action of potassium carbonate, or better, dilute sulphuric acid, on an acetone solution of pristimerin. The product contained one methoxyl group, two active hydrogen atoms, and three *C*-methyl groups. On the basis of its absorption spectrum (log $\varepsilon_{max.}$ 3·48 at 285 mμ, and log $\varepsilon_{min.}$ 2·73 at 257 mμ), the compound was formulated as a substituted catechol. It gave a green ferric reaction and a negative Gibbs reaction, an alkaline solution darkened rapidly in air, and the R_F value of the product on paper was markedly decreased in the presence of borate.[4] The infrared spectrum (Nujol) showed bands at 3460 (OH),

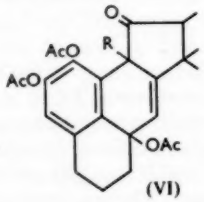


Absorption spectra of pristimerin (A) and its hydrogen chloride adduct (B).

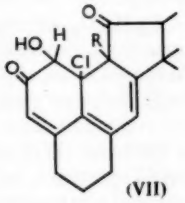
3340 (bonded OH), 1715 (bonded inert >CO), and 1701 cm.$^{-1}$ (the acetonyl-carbonyl group). In chloroform solution, a carbonyl band at 1705 cm.$^{-1}$ was obtained with a shoulder at 1724 cm.$^{-1}$. It will be evident that the presence of the acetonyl group prevents the migration of the angular methoxyl or methyl group and the double-bond rearrangements which are involved in the formation of compound (III) from pristimerin by the action of dilute sulphuric acid in the absence of acetone.



(V)



(VI)



(VII)

The dual reaction of pristimerin with dilute sulphuric acid in the presence or absence of acetone is somewhat paralleled by its reactions with acetylating agents. It has been shown in the previous paper that the naphthalene derivative (IV) is the product obtained on Thiele acetylation. With acetic anhydride in pyridine a pale yellow amorphous acetate is formed which is a benzenoid derivative (log $\varepsilon_{max.}$ 2·92 at 265 mμ) and which shows maxima in its infrared spectrum at 1776 (>CO of aromatic acetate) and 1730 cm.$^{-1}$ (inert >CO group together with >CO of aliphatic acetate). The product possibly contains some

[3] Cairns, Carboni, Coffman, Engelhardt, Heckart, Little, McGeer, McKusick, and Middleton, *J. Amer. Chem. Soc.*, 1957, **79**, 2340.
[4] Swain, *Biochem. J.*, 1953, **53**, 200.

of the triacetate (VI; R = OMe or Me), but further speculation must await the isolation of a crystalline compound.

Another type of addition has been encountered in the action of dry hydrogen chloride on pristimerin. This was originally carried out when the possibility of pristimerin's being an anhydro-base was under consideration, but the red adduct obtained, $C_{30}H_{41}O_4Cl$, contained no ionic chlorine. It was insoluble in water and gave a green ferric reaction similar to that of pristimerin, which compound it re-formed after treatment with alkali. No ketonic derivatives could be obtained and the ultraviolet and visible absorption spectrum was sufficiently close to that of pristimerin (see Figure) to suggest that the chromophore had undergone little change.

The infrared spectrum of the hydrogen chloride adduct showed strong bands at 3400 (OH), 1724 (inert >CO; chloroform solution), and 1624 cm.$^{-1}$ (unsaturated >CO of the chromophore). In view of the modified positions of the bands associated with the functional groups of the quinonoid ring, the adduct is formulated as (VII; R = OMe or Me) in which the main conjugated system of the chromophore has been maintained but the strong interaction between the hydroxyl group and the adjacent carbonyl group is apparently diminished.

Oxidative degradations of pristimerin have given further support to the proposed pristimerin structure and will be reported later.

Experimental

Methylation of Pristimerin in the Presence of Acetone.—A solution of pristimerin (700 mg.) in acetone (80 c.c.) was heated under reflux with dimethyl sulphate (2·5 c.c.) and potassium carbonate (1 g.) for 4 hr. Additional dimethyl sulphate (2 c.c.) and potassium carbonate were added, and heating was continued until there was no further reduction in the colour of the solution. The mixture was diluted with water, the acetone removed under reduced pressure, and the solution shaken with aqueous 10% sodium hydroxide to destroy the excess of dimethyl sulphate. A concentrate of an ethereal extract of the reaction product was chromatographed on alumina (grade I), and the crude methyl ether (80 mg.) crystallised from the ether eluate. Recrystallisation from aqueous methanol gave colourless needles of " methylated pristimerin," [2] m. p. 185—186° (lit., 186°) (Found: C, 76·0, 76·0, 76·65; H, 8·8, 8·9, 8·9; OMe, 18·6. Calc. for $C_{35}H_{50}O_5$: C, 76·3; H, 9·15; OMe, 16·9%), $\lambda_{max.}$ 281—282 mμ (log ε 3·35), $\lambda_{min.}$ 254—255 mμ (log ε 2·76), infrared absorption bands (in Nujol) at 1732(s), 1713(s) [1708(s) with a shoulder at 1720 in $CHCl_3$ solution], 1588, 1376(s), 1328(w), 1316, 1257, 1221, 1195, 1158(s), 1123(w), 1100(s), 1067, 1038, 1000, 861, 845, and 771 cm.$^{-1}$. The 2 : 4-dinitrophenylhydrone formed yellow needles, m. p. 204° (lit.,[2] 206°) (with previous shrinking) from ethanol (Found: C, 67·4; H, 7·7; N, 7·75. Calc. for $C_{41}H_{54}O_8N_4$: C, 67·4; H, 7·45; N, 7·7%), $\lambda_{max.}$ 362—366 and 266—268 mμ (log ε 4·34 and 4·07), $\lambda_{min.}$ 296—297 and 248—249 mμ (log ε 3·33 and 4·03), infrared bands (in Nujol) at 3330(w), 1735(s) and 1718(s) [single band at 1718(s) in $CHCl_3$ solution], 1618(s), 1600(s), 1513, 1333(s), 1314, 1284, 1270, 1240, 1205, 1137, 1093(s), 1025(w), 1005, 977, 920, and 830 cm.$^{-1}$.

Rearrangement of Pristimerin with Dilute Sulphuric Acid in the Presence of Acetone.—A solution of pristimerin (1·01 g.) in acetone (80 c.c.) was heated under reflux with 2N-sulphuric acid (30 c.c.) for 40 min. in an atmosphere of nitrogen. The initial deep red solution formed after addition of the acid was rapidly discharged to give a final straw-coloured solution. The acetone was removed under reduced pressure and the resulting precipitate was extracted with ether. The washed ethereal extracts were evaporated and the residue (1·1 g.) crystallised on trituration with ether. Repeated crystallisation from ether and finally ether–light petroleum (b. p. 40—60°) gave colourless needles (400 mg.) of the rearrangement *product*, m. p. 250° (Found: C, 75·7, 75·8, 76·0, 75·5; H, 8·5, 8·5, 8·55, 8·9; OMe, 7·2; *C*-Me, 8·7; active H, 0·43. $C_{33}H_{46}O_5$ requires C, 75·8; H, 8·9; 1OMe, 5·9; 3*C*-Me, 8·4; 2H, 0·38%), $\lambda_{max.}$ 285 mμ (log ε 3·49), $\lambda_{min.}$ 257 mμ (log ε 2·83), infrared bands (in Nujol) at 3540, 3420(s), 1715(s), and 1701(s) [band at 1705(s) with a shoulder at 1720 in $CHCl_3$ solution], 1623, 1513, 1345, 1295, 1265(w), 1219, 1163, 1094, 1060, 1027, 1000, 958(w), 861(s), and 773 cm.$^{-1}$. Paper chromatography with the butan-1-ol–water system on Whatman No. 1 paper gave R_F 0·89, and on Whatman No. 1 borate-buffered paper R_F 0·71. The product was detected with tetrazotised benzidine.

XUM

The reaction was repeated several times with methanol, dioxan, and ethyl methyl ketone as solvent in place of acetone, but in no case was the above rearrangement product isolated.

Action of Potassium Carbonate on Pristimerin in the Presence of Acetone.—Potassium carbonate (2 g.) was added to a solution of pristimerin (300 mg.) in acetone (50 c.c.), and the mixture heated under reflux for 10 hr., then diluted with water. The acetone was removed under reduced pressure, the resulting precipitate extracted into ether, and the ethereal layer washed with water and evaporated to dryness, to leave an almost colourless residue (330 mg.). The product was redissolved in ether and crystallised by slow evaporation of the solvent. Repeated recrystallisation from ether and finally ether–light petroleum (b. p. 40—60°) gave colourless needles (50 mg.) of the rearrangement product, m. p. and mixed m. p. with the compound obtained in the previous experiment, 250°.

Methylation of the Above Rearrangement Product.—A solution in acetone (25 c.c.) of the product (60 mg.) from the foregoing rearrangement was heated under reflux with dimethyl sulphate (1·5 c.c.) and potassium carbonate (1 g.) for 9 hr. Dilution with water and removal of the acetone under reduced pressure precipitated the methyl ether (64 mg.), which crystallised from aqueous methanol as colourless needles, m. p. and mixed m. p. with the direct methylation product of pristimerin, 185—186° (Found: C, 76·4, 76·2; H, 9·0, 8·95. Calc. for $C_{35}H_{50}O_5$: C, 76·3; H, 9·15%). The ultraviolet and infrared absorption spectra were identical with those of the direct methylation product.

Acetylation of Pristimerin.—A solution of pristimerin (100 mg.) in pyridine (2 c.c.) and acetic anhydride (10 c.c.) was heated under reflux for 2 hr., then poured into ice-water (100 c.c.), and the yellow precipitate (80 mg.) separated. This was soluble in light petroleum, benzene, ether, chloroform, and methanol but did not crystallise satisfactorily. Purification was effected by chromatography of an ethereal solution on silica, followed by repeated reprecipitation of the product from the ether eluate from a boiling methanolic solution by the addition of sufficient warm water to produce turbidity. The product was a pale yellow amorphous powder, m. p. 120—123°. Qualitative light absorption: $\lambda_{max.}$ 265—266 mμ; $\lambda_{min.}$ 260 mμ. Infrared absorption (Nujol): 1775(s), 1730(s), 1655(w), 1605, 1307, 1213(s), 1190, 1155, 1096, 1060(s), 975, 913, 894, and 733 cm.$^{-1}$.

Hydrogen Chloride Addition Product of Pristimerin.—Dry hydrogen chloride was passed into pristimerin (120 mg.), suspended in dry ether (15 c.c.). A deep red colour developed immediately and scarlet-red crystals (80 mg.) separated. Crystallisation from dry ethereal hydrogen chloride gave red needles of the *adduct*, m. p. 123—124° (Found: C, 71·0, 70·8; H, 8·5, 8·6; OMe, 8·8; Cl, 7·4. $C_{36}H_{41}O_4Cl$ requires C, 71·9; H, 8·2; 1OMe, 6·2; Cl, 7·1%), $\lambda_{max.}$ 420—430, 333—334, 317—318, and 238—239 mμ (log ε 4·03, 3·24, 3·12, and 4·28 respectively), $\lambda_{infl.}$ 282—283 mμ (log ε 3·32), $\lambda_{min.}$ 338, 315, and 219—220 mμ (log ε 3·21, 3·11, and 4·15), infrared bands (in Nujol): 3400, 2400(w), 1734, and 1701(s) (single band at 1724 in $CHCl_3$ solution), 1625, 1584(w), 1527, 1310, 1250, 1220, 1155, 1096, 990(w), 875(s), 853, and 780 cm.$^{-1}$.

Hydrolysis. The adduct (50 mg.) was suspended in aqueous 10% sodium hydroxide (15 c.c.) and heated under reflux for ½ hr. Acidification gave a yellow precipitate which was extracted into ether. The ethereal layer was washed and evaporated to dryness. The residue did not crystallise and a 56-transfer counter-current distribution was carried out with the solvent system used in the isolation of pristimerin.[1] Colour peaks appeared at tube numbers 0—1 and 22—24. The product isolated from tubes 23 and 24 (K 0·7) crystallised and had m. p. and mixed m. p. with pristimerin, 212°. In view of the low m. p. (pure pristimerin has m. p. 219—220°), the acetate of pristimerol was prepared by reductive acetylation:[1] it had m. p. and mixed m. p. with diacetyldihydropristimerin, 251—252°. Tubes 0—1 contained a red-brown compound, very soluble in methanol, which could not be purified.

We acknowledge the award of a Travelling Scholarship from the University of New Zealand and a maintenance grant from Professor Sir Alexander Todd (to P. K. G.).

THE UNIVERSITY, NOTTINGHAM. [*Received, June 17th*, 1957.]

938. *The Reaction of Sulphinyl Chlorides with Zinc.*

By D. Barnard.

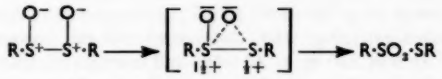
Aryl and alkyl sulphinyl chlorides react readily with zinc, to give good yields of the corresponding thiolsulphonates instead of the expected disulphoxides.

The controversy over the constitution of the so-called disulphoxides (I) has been resolved in favour of the thiolsulphonate structure (II) (for spectroscopic evidence and literature survey see Cymerman and Willis [1]) and no authenticated example of (I) appears to be known.

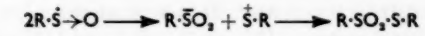
(I) R·SO·SO·R R·SO$_2$·S·R (II)

Benzenesulphenyl chloride reacts with zinc,[2] and toluenesulphonyl chloride with potassium,[3] to yield diphenyl disulphide and ditolyl disulphone respectively, and it therefore seemed possible that the highly reactive sulphinyl chlorides would undergo a similar coupling reaction to give (I). However benzenesulphinyl chloride reacted smoothly with zinc to give, not diphenyl disulphoxide, but phenyl benzenethiolsulphonate (II; R = Ph) in quantitative yield; and ethanesulphinyl chloride similarly gave ethyl ethanethiolsulphonate (II; R = Et) as the major product.

These results might be explained either by (*a*) the re-arrangement of the initially formed disulphoxide into the more stable thiolsulphonate:



or (*b*) oxygen transfer between sulphinyl radicals with subsequent coupling of the resulting sulphonyl and sulphenyl radicals, although in this case the concomitant formation of disulphide and disulphone would be expected. However di-*p*-chlorophenyl disulphide present during the reaction of zinc with benzenesulphinyl chloride was recovered as a mixed *p*-chlorophenyl phenyl disulphide although no exchange of sulphenyl groups occurred between the disulphide and phenyl benzenethiolsulphonate under the same conditions. The opposing evidence for the formation of free sulphenyl radicals in the reaction can be reconciled by the hypothesis that the transfer of negatively charged oxygen from one sulphinyl radical to a like radical occurs to give ions, or an ion pair, with a unique mode of coupling, the interaction of either of the ionic species with a disulphide resulting in the observed interchange of sulphenyl groups:



Experimental

Benzenesulphinic Acid.—Benzenesulphonyl chloride (44 g.), anhydrous sodium sulphite (63 g.), and water (300 ml.) were shaken together for 2 hr., the pH being maintained at 8—9 by periodical addition of 50% sodium hydroxide solution. The resulting solution was acidified

[1] Cymerman and Willis, *J.*, 1951, 1332.
[2] Lecher and Holschneider, *Ber.*, 1924, **57**, 755.
[3] Pearl, Evans, and Dehn, *J. Amer. Chem. Soc.*, 1938, **60**, 2478.

at 0° with 60% sulphuric acid until precipitation of the sulphinic acid was imminent. Sodium sulphate was filtered off, the filtrate diluted with water (40 ml.), and the acidification completed, to give the sulphinic acid (23 g.) which, after being washed with a little ice-water and dried at 0° *in vacuo* for 1 day over phosphoric oxide was virtually free from sodium sulphate and had m. p. 83—84°.

Benzenesulphinyl Chloride.—Purified thionyl chloride (14 ml.) was added slowly with stirring to freshly prepared benzenesulphinic acid (12 g.) suspended in dry ether (50 ml.) at 0°. Dry benzene (25 ml.) was added and the solvent and excess of thionyl chloride distilled at 10 mm. into a liquid-air trap. This operation was repeated with an equal volume of benzene, leaving the sulphinyl chloride in almost quantitative yield. Distillation of the product in a high vacuum occasionally led to an almost explosive decomposition and was not therefore generally attempted.

Reaction of Benzenesulphinyl Chloride with Zinc.—The chloride was added in dry ether (50 ml.) slowly to a stirred suspension of zinc powder (6 g.) in ether (50 ml.) at room temperature. The mixture became slightly warm and was kept overnight. Isolation of the product in the usual manner gave phenyl benzenethiolsulphonate (10·15 g., 96%), m. p. 33—35° which, after one crystallisation from 10 : 1 light petroleum (b. p. 40—60°)–ethanol, had m. p. and mixed m. p. 37·5—38·5° (Found: C, 57·5; H, 4·0; S, 25·6. Calc. for $C_{12}H_{10}O_2S_2$: C, 57·6; H, 4·0; S, 25·6%). Other specimens of this thiolsulphonate prepared by the following methods: (*a*) oxidation of diphenyl disulphide by peracetic acid and by ozone, (*b*) thermal decomposition of benzenesulphinic acid and (*c*) disproportionation of phenyl benzenethiolsulphinate, also had this m. p. (N.P.L. standard thermometer; uncorr.), unchanged by further crystallisation from light petroleum or aqueous ethanol, as opposed to the values 42—46° quoted in the literature. All specimens were spectrally identical with that described by Cymerman and Willis [1] of m. p. 45°.

Reaction of Benzenesulphinyl Chloride with Zinc in the Presence of Di-p-chlorophenyl Disulphide.—Benzenesulphinyl chloride (4·8 g.) was treated with zinc (2 g.) as above in the presence of di-*p*-chlorophenyl disulphide (2·0 g.). The disulphide was extracted from the oily product with light petroleum (b. p. 60—80°, 50 ml.) an aliquot part (10 ml.) of which was then run down a column of silica gel (20 g., 100—200 mesh) and the disulphide eluted with carbon tetrachloride (150 ml.). It now had m. p. 45—56° and from its analysis disclosed 18·8 moles % of phenyl groups (Found: C, 52·7; H, 3·1; S, 23·3; Cl, 21·1. Calc. for $C_{12}H_{8\cdot38}S_2Cl_{1\cdot62}$: C, 52·6; H, 3·1; S, 23·3, Cl, 21·0%). No sulphenyl group interchange was observed when equimolar amounts of di-*p*-chlorophenyl disulphide and phenyl benzenethiolsulphonate were (*a*) melted together at 75° for 30 min., (*b*) kept in carbon tetrachloride solution for 24 hr. at 20°, and (*c*) kept in ether in the presence of an equimolar amount of zinc chloride for 24 hr. at 20°. Only slight interchange (6 moles %) occurred when a solution of the two components in benzene was irradiated with light from a mercury-vapour lamp for 3 hr.

Ethanesulphinyl Chloride.—This compound [4] had b. p. 47·5—48·5°/11 mm., n_D^{20} 1·4978 (Found: C, 21·5; H, 4·8; S, 28·7; Cl, 32·2. Calc. for C_2H_5OSCl: C, 21·3; H, 4·5; S, 28·5; Cl, 31·6%).

Ethyl Ethanethiolsulphonate.—Chlorination of diethyl disulphide (37 g.) in acetic acid (160 ml.) containing water (23·5 g.) essentially according to the method of Lee and Dougherty [5] gave ethyl ethanethiolsulphonate (28·5 g.) as the major product together with ethanesulphonyl chloride (16·8 g.). The thiolsulphonate had b. p. 70°/0·02 mm., n_D^{20} 1·4988 (Found: C, 31·4; H, 6·5; S, 41·4. Calc. for $C_4H_{10}O_2S_2$: C, 31·2; H, 6·5; S, 41·6%), with characteristic sulphone absorption bands in the infrared region at 1338 cm.$^{-1}$ (ε 616) and 1139 cm.$^{-1}$ (ε 808).[6]

Reaction of Ethanesulphinyl Chloride with Zinc.—The chloride (12·9 g.) in dry ether (50 ml.) was added slowly to a stirred suspension of zinc powder (12 g.) in ether (50 ml.) at 20°. The yellow oil isolated (7·12 g.) was mainly ethyl ethanethiolsulphonate (88% purity by infrared spectroscopy) and fractionation gave an almost pure sample (4·8 g.; 95% purity), b. p. 70°/0·02 mm., n_D^{20} 1·4998 (Found: C, 31·0; H, 6·5; S, 42·0%). Reaction at 0° gave only a 50% yield of thiosulphonate and the infrared spectrum of the total product indicated the presence of a component with absorption in the sulphoxide region at 1118 cm.$^{-1}$. The shift in frequency from a simple dialkyl sulphoxide (*ca.* 1050 cm.$^{-1}$) would be in keeping with the expected properties of

[4] Douglass and Poole, *J. Org. Chem.*, 1957, **22**, 536.
[5] Lee and Dougherty, *ibid.*, 1940, **5**, 81.
[6] Evans and Higgins, unpublished work.

a disulphoxide [6] (cf. ethyl ethanethiolsulphinate, 1093 cm.$^{-1}$, and ethanesulphinyl chloride, 1159 cm.$^{-1}$). The substance decomposed on attempted isolation.

This work forms part of a programme of research undertaken by the Board of the British Rubber Producers' Research Association.

BRITISH RUBBER PRODUCERS' RESEARCH ASSOCIATION,
48–56, TEWIN ROAD, WELWYN GARDEN CITY, HERTS. [*Received, June 28th*, 1957.]

NOTES.

939. *The Spontaneous Decomposition of Aryl Thiolsulphinates.*

By D. BARNARD.

BACKER and KLOOSTERZIEL [1] have reported the occasional spontaneous disproportionation of thiolsulphinates into thiolsulphonates and disulphides:

$$2R{\cdot}SO{\cdot}S{\cdot}R \longrightarrow R{\cdot}SO_2{\cdot}S{\cdot}R + R{\cdot}S{\cdot}S{\cdot}R$$

A number of aryl thiolsulphinates have been prepared by the method of these authors and found to be stable for several months under normal atmospheric conditions but to undergo rapid decomposition *in vacuo*. Thus *p*-tolyl benzenethiolsulphinate, which was particularly sensitive in this respect, decomposed after five minutes at 10^{-5} mm. and after one hour at 10^{-2} mm.; the corresponding times for *p*-chlorophenyl benzenethiolsulphinate were one and eight hours. The decomposition was made evident by sudden melting of the sample; no detectable loss in weight occurred and the rise in temperature was small (*ca.* 20°). Similar decomposition took place after longer periods of storage over phosphoric oxide, suggesting that in each case the stringent drying was responsible. An explanation might be that the destabilising effect of the highly polar S→O group on the thiolsulphinate molecule (the yellow colour of aryl thiolsulphinates suggesting charge separation within the molecule) is lessened by strong intermolecular bonding in the crystal lattice, the boundary molecules partially satisfying their bonding requirements by hydrogen-bond formation with absorbed water. On removal of the latter the decomposition of the surface molecules, possibly initiated photochemically, is propagated throughout the crystal either by a free-radical or ionic chain process or simply by the destabilisation of successive layers of molecules.

Thiolsulphinates carrying unlike aryl groups did not give an equimolar yield of di-

Products of decomposition of thiolsulphinate Ph·SO·S·Ar'.

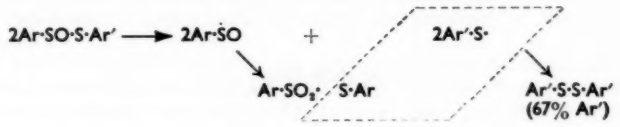
Ar'	Products (mole %) Disulphide	Thiolsulphonate	Sulphonic acid	Ar' group in disulphide (mole %)
Ph	51	46	—	—
p-Tolyl	57	43	7	64
p-Cl·C$_6$H$_4$	62·5	30	16	67

sulphide and thiolsulphonate, and a third substance, isolated in the examples studied as benzenesulphonic acid, was a minor product. The disulphide and acid contents shown in the Table are considered accurate to $\pm 1\%$, but separation of thiolsulphonate was complicated by the presence of acidic material and no effort was made to improve the

[1] Backer and Kloosterziel, *Rec. Trav. chim.*, 1954, **73**, 129.

accuracy of recovery beyond ± 10%. It is difficult to visualise the formation of free benzenesulphonic acid and the infrared spectra of freshly decomposed thiolsulphinates confirmed the absence of hydroxyl groups. It must be assumed, therefore, that the sulphonic acid is formed by hydrolysis of an anhydride during the isolation procedure.

Now it has been shown that exchange of sulphenyl groups between disulphides and thiolsulphonates does not occur under the experimental conditions,[2] so the composition of the disulphides suggests that disproportionation of the thiolsulphinates does not involve



a simple oxygen transfer and that breaking of the S–S bond is an essential step. If this is assumed to be a homolytic cleavage to sulphinyl and sulphenyl radicals, then thiolsulphonate would be derived from the former radicals [2] and a mixed disulphide from the sulphenyl radicals after their equilibration with the sulphenyl group of the thiolsulphonate.

Experimental.—The thiolsulphinates were prepared by the method of Backer and Kloosterziel [1] and crystallised to constant m. p. by cooling solutions in chloroform–light petroleum (b. p. 30—40°) (1 : 30), saturated at room temperature, to −10°. Phenyl benzenethiolsulphinate had m. p. 69—70° (Found: C, 61·4; H, 4·2; S, 27·3. Calc. for $C_{12}H_{10}OS_2$: C, 61·5; H, 4·3; S, 27·4%). *p*-Tolyl benzenethiolsulphinate had m. p. 70·0—70·2° (Found: C, 62·7; H, 5·0; S, 25·7. Calc. for $C_{13}H_{12}OS_2$: C, 62·9; H, 4·8; S, 25·8%). *p-Chlorophenyl benzenethiolsulphinate* had m. p. 61—62° (Found: C, 53·8; H, 3·5. $C_{12}H_9OS_2Cl$ requires C, 53·6; H, 3·4%).

Isolation of the products of decomposition. The following procedure was typical. *p*-Tolyl benzenethiolsulphinate (1·1935 g.) was kept at 10^{-5} mm. until decomposition occurred (5 min.), to give a yellow oil (1·1933 g.), a portion of which (0·6277 g.), dissolved in carbon tetrachloride (50 ml.), was absorbed on a silica gel column (20 × 1 cm.; 20 g.; 100—120 mesh). Elution with carbon tetrachloride (150 ml.) and then chloroform (200 ml.) gave respectively, after removal of the solvents, disulphide (0·3407 g.) [Found: C, 67·5; H, 5·4; S, 27·1. Calc. for $C_{14}H_{14}S_2$ (64 mole %) + $C_{12}H_{10}S_2$ (36 mole %): C, 67·5; H, 5·3; S, 27·1%)] and thiolsulphonate (0·2870 g.; purity by infrared spectroscopy 96%) contaminated with acidic material. The original material (0·5395 g.) required 8·0 ml. of 0·0213N-sodium hydroxide for neutrality to screened methyl-red. A larger quantity of the thiolsulphinate (10·41 g.) was similarly decomposed and the products extracted with water. The aqueous solution was neutralised and evaporated to small volume (2 ml.). Addition of benzyl*iso*thiuronium chloride (0·3 g.) in water (1 ml.) gave an immediate precipitate (0·24 g.), m. p. 140—142·5°, which after one crystallisation from light petroleum (b. p. 60—80°)–ethanol had m. p. and mixed m. p. with authentic benzyl*iso*thiuronium benzenesulphonate 145·5—146·5°.

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[*Received, June 28th,* 1957.]

[2] Barnard, preceding paper.

940. *The Resolution of* 3 : 5-*Dimethylhex*-1-*yn*-3-*ol. The Reduction of its* (+)-*Isomeride to* (−)-3 : 5-*Dimethylhexan*-3-*ol.*

By J. R. Hickman and J. Kenyon.

Although the brucine salt of (+)-3 : 5-dimethylhex-1-yn-3-yl hydrogen phthalate is much less soluble than its diastereoisomeride, their separation by fractional crystallisation proved slower than expected—owing, possible, to adsorption of the more soluble salt on the crystals of the less soluble. This behaviour was not encountered in the resolution of 3-methylpent-1-yn-3-ol.[1]

The specific rotatory powers of the (+)-hydrogen phthalate have been determined in a number of solvents (see Table 1); the values are all of the same sign and, for a given wavelength, cover a relatively restricted range.

Table 1.

Specific rotatory powers of (+)-3 : 5-*dimethylhex*-1-*yn*-3-*yl hydrogen phthalate in various solvents* (*l*, 1; *c*, 10·00).

Solvent	Temp.	$[\alpha]_{4358}$	$[\alpha]_{4800}$	$[\alpha]_{5086}$	$[\alpha]_{5461}$	$[\alpha]_{5780}$	$[\alpha]_{5893}$
EtOH	24°	+106°	+75·3°	+65·4°	+54·4°	+47·1°	+45·5°
Et_2O	24	82·5	60·0	51·6	41·8	37·3	34·0
Dioxan	23	53·1	38·8	33·2	27·4	24·8	22·2
Acetone ...	24	80·4	58·6	50·9	40·8	35·6	34·8
Pyridine ...	23	66·2	46·4	42·5	33·8	30·7	26·3
$CHCl_3$	23	67·3	48·8	44·3	35·6	32·1	29·5
C_6H_6	24	47·0	43·9	36·5	30·0	27·2	25·5
EtOAc	23	78·6	58·0	50·2	40·5	36·5	33·1

Specific rotatory powers of (−)-3 : 5-*dimethylhex*-1-*yn*-3-*yl* p-*nitrobenzoate* (*l*, 1; *c*, 7·9).

		$[\alpha]_{4800}$	$[\alpha]_{5086}$	$[\alpha]_{5461}$	$[\alpha]_{5780}$	$[\alpha]_{5893}$	$[\alpha]_{5438}$
Benzene.....	21°	−71·0°	−60·4°	−41·1°	−40·9°	−36·1°	−37·7°

Despite this uniformity of optical behaviour, the (−)-hydrogen phthalate yielded, on hydrolysis, the (+)-alcohol, which in turn gave a (−)-*p*-nitrobenzoate. This acetylenic alcohol was readily hydrogenated to the saturated lævorotatory alcohol.

The rotatory power of the saturated alcohols obtained (*a*) by direct resolution[2] (α^{21}_{5893} −2·26°) and (*b*) (α^{20}_{5893} −2·65°) by reduction of the acetylenic alcohol are in close agreement,

Table 2.

Observed rotatory powers of (−)-3 : 5-*dimethylhex*-1-*yn*-3-*ol at* 20° (*l*, 1).

α_{4358}	α_{4800}	α_{5086}	α_{5461}	α_{5780}	α_{5893}	α_{6438}
−2·22°	−1·58°	−1·47°	−1·44°	−1·19°	−1·26°	−1·08°

Observed rotatory powers of (−)-3 : 5-*dimethylhexan*-3-*ol* (*optical purity* 40%) *at* 19° (*l*, 1).

α_{4358}	α_{4800}	α_{5086}	α_{5461}	α_{5780}	α_{5893}
−2·46°	−1·79°	−1·52°	−1·41°	−1·24°	−0·99°

suggesting that both the saturated and the unsaturated alcohol have been obtained virtually optically pure. Further evidence for this is provided by an independent resolution of the saturated alcohol in this laboratory by Salamé[3] which gave the value α^{20}_{5893} −2·72°.

[1] Hickman and Kenyon, *J.*, 1955, 2051.
[2] Doering and Zeiss, *J. Amer. Chem. Soc.*, 1948, **70**, 3966.
[3] Salamé, Ph.D. Thesis, London, 1955.

Experimental.—(±)-3 : 5-Dimethylhex-1-yn-3-ol was obtained by distillation of a commercial sample, the middle fraction of b. p. 150—151°, d_{20}^{20} 0·8597, n_D^{20} 1·4350, being used (Found: C, 76·1; H, 11·2. Calc. for $C_8H_{14}O$: C, 76·2; H, 11·1%).

(±)-3 : 5-*Dimethylhex*-1-*yn*-3-*yl hydrogen phthalate*. The alcohol (35 g.), phthalic anhydride (40 g.), and triethylamine (20 g.) were heated at 90° for 2 hr., then treated with cold dilute hydrochloric acid and extracted with ether. The extract was washed with dilute acid, then with aqueous sodium carbonate; the sodium carbonate extracts were shaken with ether, then acidified, and the liberated *ester* extracted with chloroform. This, after drying and removal of the solvent, yielded the crude ester (59 g., 79%) which separated from aqueous ethanol (charcoal) in rhombs, m. p. 111—112° [Found: C, 70·1; H, 6·6%; *M* (by titration with KOH), 274. $C_{16}H_{18}O_4$ requires C, 70·1; H, 6·6%; *M*, 274].

Resolution. The (±)-phthalate (50 g.) and anhydrous brucine (73·5 g.) were dissolved in the minimum quantity (750 c.c.) of boiling acetone, and the solution allowed to cool. The crystals which had separated during 2 days were recrystallised thrice from acetone, thus becoming almost insoluble in the boiling solvent. They were then heated under reflux with acetone and the procedure repeated four times with fresh solvent. The resulting crystals were recrystallised from benzene in which they were appreciably more soluble. The last two crops of brucine salt, rhombs, m. p. 183—184°, after decomposition with acid, yielded (+)-3 : 5-*dimethylhex*-1-*yn*-3-*yl hydrogen phthalate* of identical rotatory powers. The last ester (17·5 g.) separated from aqueous ethanol in rhombs, m. p. 61—62° (Found: *M*, 273). Rotatory powers are in Table 1.

A mixture of the more soluble fractions of brucine salt produced as above was decomposed with dilute hydrochloric acid, and the liberated acid ester extracted with ether. After removal of the ether, this had m. p. 102—104° and $[\alpha]_{5893}^{20}$ −11·2° (*c*, 10·00; *l*, 1) in C_6H_6: after seven recrystallisations from benzene–light petroleum, the (−)-*hydrogen phthalate* was optically pure, forming rhombs, m. p. 63—65°, $[\alpha]_{5893}^{20}$ −24·9° (*c*, 10·00; *l*, 1) in C_6H_6 (Found: *M*, 272).

(−)-3 : 5-*Dimethylhex*-1-*yn*-3-*ol*. The (+)-hydrogen phthalate (16·0 g.) was heated with a slight excess of methanolic potassium hydroxide, and the liberated alcohol removed in steam; the distillate was saturated with salt and extracted with ether. The resulting (−)-3 : 5-*dimethylhex*-1-*yn*-3-*ol* (5·2 g.) had b. p. 150—151°/760 mm., 56—57°/19 mm., d_{20}^{20} 0·8594, n_D^{20} 1·4348 (Found: C, 76·1; H, 11·0%). Rotatory powers are in Table 2.

(±)-3 : 5-*Dimethylhex*-1-*yn*-3-*yl* p-*nitrobenzoate*. The (±)-alcohol (1·4 g.), *p*-nitrobenzoyl chloride (1·9 g.), and pyridine (3 g.), after 5 min. on the steam bath, gave this *ester*, needles (1·2 g.) (from aqueous ethanol), m. p. 52—53° (Found: C, 65·5; H, 6·4; N, 5·1. $C_{15}H_{17}O_4N$ requires C, 65·0; H, 6·8; N, 5·1%).

The (−)-*ester*, similarly prepared from the (+)-alcohol, formed needles (from aqueous ethanol), m. p. 53—54° (Found: C, 65·4; H, 6·2; N, 5·1%). Rotatory powers are in Table 1.

(±)-2-(3 : 5-*Dimethylhex*-1-*yn*-3-*yl*) 1-*hydrogen* 3-*nitrophthalate*. The (±)-alcohol (2 g.), 3-nitrophthalic anhydride (2·8 g.), and pyridine (3 g.), after 1 hr. on the steam-bath, were worked up as above. The resulting *ester* (2·3 g.) separated from aqueous ethanol in rhombs, m. p. 145—146° [Found: C, 60·0; H, 5·2; N, 4·4%; *M* (by titration), 316. $C_{16}H_{17}O_6N$ requires C, 60·2; H, 5·3; N, 4·4%; *M*, 319]. The structure of this ester is based on the usual behaviour of 3-nitrophthalic anhydride when heated with alcohols.

Reduction of (+)-3 : 5-*dimethylhex*-1-*yn*-3-*ol to* (−)-3 : 5-*dimethylhexan*-3-*ol*. (+)-3 : 5-Dimethylhex-1-yn-3-ol, α_{5893}^{20} +0·50° (*l*, 1) (optical purity 40%) (5 g.), in ether (100 c.c.) was shaken with hydrogen (palladium–charcoal) until no more was absorbed. After filtration and distillation, the resulting (−)-3 : 5-dimethylhexan-3-ol (2·1 g.) had b. p. 150—151°/760 mm., d_{20}^{20} 0·8344, n_D^{18} 1·4271 (Found: C, 73·0; H, 13·6. Calc. for $C_8H_{18}O$: C, 73·8; H, 13·8%). Rotatory powers are in Table 2.

Thanks are expressed to the Central Research Fund Committee of London University for a Grant.

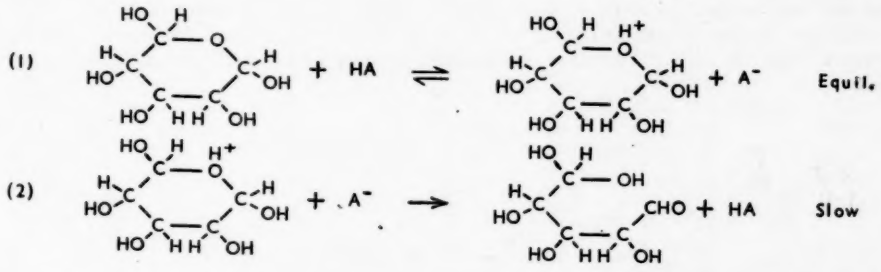
BATTERSEA POLYTECHNIC, LONDON, S.W. 11. [*Received, April 30th,* 1957.]

941. *Relative Rates of Mutarotation of Tetra-O-methyl-α-D-glucose in H_2O and D_2O and the Mechanism of the Reaction.*

By B. C. Challis, F. A. Long, and Y. Pocker.

The most probable mechanism for the acid catalysed mutarotation of glucose and similar sugars involves protonation of the ether-oxygen atom, followed by attack of a base on the alcohol proton with simultaneous ring opening.[1] This is, of course, a case of general acid-catalysis. A somewhat similar mechanism presumably holds for the observed general base-catalysis.

A frequent test for the existence of a pre-equilibrium proton transfer of the type of step (1) is a study of the relative rates of reaction in the solvents deuterium oxide and water. Data for such studies with glucose are listed in Table 1. The $(k_H/k_D)_{H^+}$ ratio for



catalysis by strong acids is greater than unity, considerably larger than is usually observed for reactions with a pre-equilibrium proton transfer. This fact has frequently led to the suggestion that the reaction does not involve a pre-equilibrium but goes by a one-step slow protonation.[2] However, an alternative explanation for the observed large ratio is that there is indeed a pre-equilibrium proton transfer, with as a consequence a relatively larger concentration of conjugate acid for the D_2O case, but that the rate of step (2) (for reaction with water as the base) is so much slower in the solvent D_2O that the effect of

Table 1. *Relative rates of mutarotation (k_H/k_D) in H_2O and D_2O at 25°.*

Catalyst	Glucose	Ref.	Tetramethylglucose
H^+	1·37	[a]	1·31
H_2O	3·80 or 3·16	[a, b]	3·2
AcOH	2·6	[a]	
AcO^-	2·38		

[a] Hamill and LaMer *J. Chem. Phys.*, 1936, **4**, 395. [b] Moelwyn-Hughes, Klar, and Bonhoeffer, *Z. Electrochem.*, 1934, **40**, 469.

step (1) is more than counterbalanced. Such a large isotope effect on the slow step does not appear to occur in other pre-equilibrium mechanisms but it is imaginable that the glucose reaction is special, possibly because glucose has five hydroxyl groups with exchangeable hydrogen atoms. To see if this last aspect of glucose is of importance we

[1] Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, 1940, Chap. XI; Ingold, "Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, Ithaca, N.Y., 1953, Chap. X.

[2] Bonhoeffer, *Trans. Faraday Soc.*, 1938, **34**, 252; Bell, "Acid–Base Catalysis," Oxford Univ. Press, 1941.

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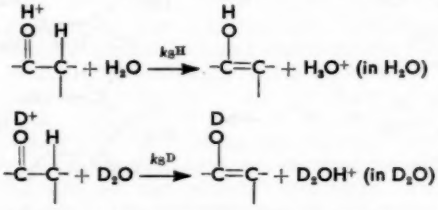
have studied the uncatalysed and the acid-catalysed mutarotation of tetra-*O*-methyl-α-D-glucose in the solvents D_2O and H_2O. Table 1 summarises the results.

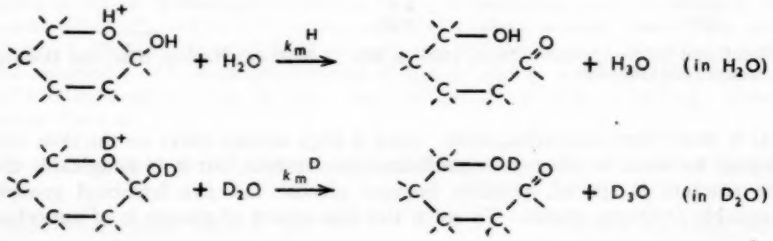
Since the results for tetramethylglucose are so similar to those for ordinary glucose, it is reasonable to conclude that the large value of k_H/k_D for catalysis by strong acids is a characteristic property of the mutarotation. The question then remains: if a pre-equilibrium proton transfer is involved, why the uniquely high $(k_H/k_D)_{H^+}$ ratio? We believe that there is a plausible answer to this question and hence that the pre-equilibrium mechanism is very probably correct.

Almost all of the many acid-catalysed reactions studied in H_2O and D_2O involve specific hydrogen-ion catalysis, not general acid-catalysis. The slow step for these reactions thus does not involve a proton transfer. Other than the glucose mutarotation, the only reaction studied which certainly shows general acid-catalysis and hence involves a slow proton transfer is the enolisation of acetone (normally studied by halogen absorption). In this case the observed $(k_H/k_D)_{H^+}$ ratio is 0·47, *i.e.*, the acid-catalysed reaction is faster in D_2O.[3] This is the expected result since it is well established from other evidence that the reaction involves a pre-equilibrium proton transfer.[4] The important thing is that here the proton which is attacked in the slow step remains unchanged for reaction in the solvents D_2O and H_2O. The rate-determining reactions for water as the base, are:



Since a C–H bond is broken in the rate step for both reactions, a value of $k_S^H/k_S^D = 1$ is reasonable. Hence the observed $(k_H/k_D)_{H^+}$ of 0·47 is a straightforward reflection of the different amounts of conjugate acid formed in the pre-equilibrium step. However, if the reaction in D_2O had involved fission of a C–D rather than of a C–H bond the rate would have been decreased enough to make the $(k_H/k_D)_{H^+}$ ratio considerably greater than unity. This follows from the fact that the acid-catalysed enolisation of $[^2H_6]$acetone in either H_2O or D_2O is slower [5] than that of ordinary acetone by a factor of 7·7.

The reason for the large $(k_D/k_H)_{H^+}$ ratio for mutarotation (on the pre-equilibrium mechanism) is now evident. The protons of hydroxyl groups are known to equilibrate instantaneously with an aqueous solvent.[6] Hence for mutarotation the slow step involves rupture of an O–H bond for reaction in H_2O and an O–D bond in D_2O, with simultaneous ring opening in both cases:



[3] Reitz, *Z. phys. Chem.*, 1937, **179**, *A*, 119.
[4] Ref. 1, chap. VIII.
[5] Reitz and Kopp, *Z. phys. Chem.*, 1939, **184**, *A*, 429.
[6] Ref. 5 gives data on this point for glucose itself.

One can thus expect a slower rate-determining step in D_2O. Even noting that much of the energy of activation for this step must come from the simultaneous ring opening, a factor of k_m^H/k_m^D of around 3 is not unreasonable. This is enough to counterbalance the effect of the pre-equilibrium and explain the observed $(k_H/k_D)_{H^+}$ ratio.*

If this explanation is valid it can be predicted that $(k_H/k_D)_{H^+}$ values for aqueous reactions which exhibit general acid-catalysis along with pre-equilibrium proton transfer will separate fairly sharply into two groups: values of about $\frac{1}{2}$ to $\frac{1}{3}$ for cases where the proton which is attacked in the slow step does not exchange with the solvent and values of 1 or larger where the proton which is attacked exchanges rapidly with the solvent.

Experimental.—2 : 3 : 4 : 6-Tetra-*O*-methyl-D-glucose was prepared in the usual manner,[7] and the α-form was recovered by repeated recrystallisation from anhydrous " pentane " (b. p. 26—40°) containing 0·5% of ether. The rate of mutarotation was followed polarimetrically in a jacketed 20 cm. polarimeter tube. The solutions contained 0·0936 g. of tetramethylglucose per ml. Rate coefficients were determined by the Guggenheim procedure.

Studies were made at 25° and at a constant ionic strength of 0·2. The spontaneous rate was measured at pH 4·7, at which contributions from terms in H^+ and OH^- are negligible; the solutions were 0·005M in sodium acetate, 0·0025M in acetic acid, and 0·195M in sodium chloride. The acid-catalysed mutarotation was studied with solutions of hydrochloric acid containing sodium chloride to give an ionic strength of 0·2. The experimental results are in Table 2.

TABLE 2.

Solvent	[HCl] (M)	$10^4k_{exp.}$ (sec.$^{-1}$)	$10^4k_{exp.}$ (average)	$k_{H^+} = (k_{exp.} - k_{H_2O})/C_{H^+}$
H_2O	(pH = 4·7)	3·42; 3·44; 3·46	3·44	—
D_2O	(pH = 4·7)	1·07; 1·06	1·065	—
H_2O	0·0585	6·22; 6·24	6·23	47·7
D_2O	0·0538	2·99	2·99	35·8
H_2O	0·115	9·06; 9·14	9·10	49·2
D_2O	0·100	4·88; 4·76	4·82	37·6
H_2O	0·173	11·74	11·74	48·0
D_2O	0·165	7·11	7·11	36·6

From the average values the ratios are $(k_H/k_D)_{H_2O} = 3·23$ and $(k_H/k_D)_{H^+} = 1·31$.

The original deuterium oxide contained 99·8 atoms % of D. There was some isotopic dilution from the added tetramethylglucose, acetic acid, and hydrochloric acid, and the extent of this differed slightly in the various runs. However, to a good approximation the quoted ratios can be taken to be for the solvents water and 99% deuterium oxide.

One of the authors (F. A. L.) is indebted to the National Science Fundation (U.S.A.) for a Fellowship during 1956—1957.

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WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES, UNIVERSITY COLLEGE, GOWER STREET, LONDON, W.C.1. [*Received, June 24th*, 1957.]

* A fairly straightforward argument can be made to show that the observed $(k_H/k_D)_{H^+}$ ratio for mutarotation is semi-quantitatively in accord with the pre-equilibrium mechanism. From the Bigeleisen procedure for treating isotope effects (*J. Chem. Phys.*, 1949, **17**, 324) one can express the ratio of rate coefficients for the slow step as $(k_m^H/k_m^D) = Fv_*^H/v_*^D$, where F is a function which involves zero-point energies of reactants and transition state and v_* is the frequency with which the transition state species moves across the barrier to give products. Since movement of H *versus* D is involved, v_*^H/v_*^D should be $\sqrt{2}$. The observed $(k_H/k_D)_{H^+}$ value will be the product of the above ratio and a term which expresses the different concentrations of the conjugate acids formed in the pre-equilibrium step. However, the latter also depends on the different zero-point energies and can be written $1/F'$ where, because for both step (1) and (2) the important change is from an OH to an OD group, $F' \simeq F$. Hence the observed ratio should be $(k_H/k_D)_{H^+} \simeq \sqrt{2}$.

[7] *Org. Synth.*, 1940, **20**, 100.

942. *The Organic Chemistry of Phosphorus. Part VI.* Some Phosphorus-containing Derivatives of 2 : 2 : 2-Trichloroethanol and N-Methylaniline.*

By H. N. Rydon and B. L. Tonge.

The experiments described below were carried out in an unsuccessful attempt to find reagents which might, in certain cases, advantageously replace triphenyl phosphite in the preparation of alkyl [1] and aryl [2] halides.

One such reagent is tris-2 : 2 : 2-trichloroethyl phosphite (I), which is readily prepared by the action of phosphorus trichloride on 2 : 2 : 2-trichloroethanol in the presence of a tertiary amine.[3] In our hands, contrary to the experience of Gerrard, Green, and Phillips,[3] omission of the base led to the formation of the phosphonate (II); the most obvious mechanism for the formation of this ester (II) is by an intramolecular Arbuzov reaction of the ester (I), but such reactions are generally slow [4] and ester (I) has been shown to be stable to hydrogen chloride under the reaction conditions; some more direct mechanism may, therefore, obtain. Gerrard, Green, and Phillips [3] state that the action

(I) $(CCl_3\cdot CH_2\cdot O)_3P$ $(CCl_3\cdot CH_2\cdot O)_2P(O)\cdot CCl_2\cdot CH_2Cl$ (II)

(III) $(CCl_3\cdot CH_2\cdot O)_3PCl_2$ $(CCl_3\cdot CH_2\cdot O)_3PO$ (IV)

of chlorine on the phosphite (I) yields the phosphate (IV), directly, " by a mechanism still obscure." Stoicheiometric considerations alone seem to preclude direct formation of a phosphate from a phosphite; the maximum possible yield in such a reaction, without intervention of any other oxygen-containing reagent, is 75%, which is the yield of phosphate actually isolated by Gerrard, Green, and Phillips, while even higher yields of phosphate from tris-1 : 1 : 1 : 3 : 3 : 3-hexachloro*iso*propyl phosphite are recorded.[5] Re-investigation of the reaction between the phosphite (I) and chlorine has shown that the first product is a dichloride, (III), or some ionic form of this,[6] which yields 1 : 1 : 1 : 2-tetrachloroethane on pyrolysis; this dichloride, which is the first trialkyl phosphite dihalide to have been isolated, gave a good yield of the phosphate (IV) on treatment with water. The dichloride (III) resembles the analogous aryl compounds [6] in being extremely susceptible to the action of moisture, mere traces of which suffice to convert it into the phosphate; there seems little doubt that the earlier workers underestimated the sensitivity of the dichloride towards moisture and were thus led to believe that the phosphate was formed directly.

Another reagent which might replace triphenyl phosphite in some of its preparative applications is phosphorous tri-(*N*-methylanilide) † $P(NMePh)_3$, which is readily prepared from phosphorus trichloride and *N*-methylaniline; it forms an addition compound with chlorine, which gives phosphoric tri-(*N*-methylanilide) $PO(NMePh)_3$ with water but is insufficiently reactive towards alcohols to be of preparative value.

* Part V, Ayres and Rydon, *J.*, 1957, 1109.

† Since our work was completed this compound has been prepared, but not purified, by Abramovitch, Hey, and Long.[7]

[1] Landauer and Rydon, *J.*, 1953, 2224; Coe, Landauer, and Rydon, *J.*, 1954, 2281.
[2] Coe, Rydon, and Tonge, *J.*, 1957, 323.
[3] Gerrard, Green, and Phillips, *J.*, 1954, 1148.
[4] Kabachnik and Rossiiskaya, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 1946, 295, 403, 515.
[5] Gerrard and Howe, *J.*, 1955, 505.
[6] Rydon and Tonge, *J.*, 1956, 3043.
[7] Abramovitch, Hey, and Long, *J.*, 1957, 1781.

Experimental.—Tris-2 : 2 : 2-trichloroethyl phosphite (I). Phosphorus trichloride (13·8 g.) was added slowly, with stirring, to 2 : 2 : 2-trichloroethanol (45 g.) and diethylaniline (45 g.) in ether (200 ml.) at 0°. After 2 hr. dimethylaniline hydrochloride (52 g., 93%) was filtered off and the filtrate distilled, affording the phosphite (33·7 g., 71%), b. p. 127—131°/0·1 mm., n_D^{20} 1·5174.

The phosphite (3 g.), containing chloral (10 mg.), was warmed to 60° while dry hydrogen chloride was passed through it for an hour. Distillation gave unchanged phosphite (2·75 g., 92%), b. p. 150—153°/3 mm., n_D^{20} 1·5173.

Bis-2 : 2 : 2-trichloroethyl 1 : 1 : 2-trichloroethyl phosphonate (II). Phosphorus trichloride (13·8 g.) was added slowly during an hour to cooled, stirred 2 : 2 : 2-trichloroethanol (45 g.). Stirring was continued for a further hour, the mixture solidifying. The product was treated with light petroleum (b. p. 40—60°) and filtered; recrystallisation of the solid (31 g., 65%), m. p. 144—146°, from chloroform–light petroleum (b. p. 40—60°) gave the *phosphonate* in fine needles, m. p. 153—154° [Found: C, 15·0; H, 1·6; P, 6·4%; *M* (Rast), 450 ± 25. $C_6H_6O_3PCl_9$ requires C, 15·2; H, 1·3; P, 6·5%; *M*, 476·5]. The compound was unchanged after treatment with chlorine or bromine in chloroform solution; hydrolysis by 4 hours' refluxing with 2N-sodium hydroxide yielded 2 : 2 : 2-trichloroethanol (1·85 mol.), characterised as its 1-naphthylurethane, m. p. and mixed m. p. 120°.

Action of chlorine on tris-2 : 2 : 2-trichloroethyl phosphite. (*a*) Chlorine was passed, with stirring, into a solution of the phosphite (9·5 g.) in anhydrous ether (50 ml.) until a faint permanent green colour appeared. The product was evaporated under reduced pressure and the solid, hygroscopic residue was treated with water. The resulting solid was recrystallised from aqueous ethanol, affording tris-2 : 2 : 2-trichloroethyl phosphate (7·3 g., 74%), m. p. 71° (lit.,[3] m. p. 72°).

(*b*) The phosphite (23·8 g.) was similarly treated with chlorine (3·6 g.); after a further hour's stirring, the bulk of the ether was removed by decantation and the residue dried *in vacuo*. The product was heated in a bath at 150°; redistillation of the volatile product gave 1 : 1 : 1 : 2-tetrachloroethane (4·5 g., 54%), b. p. 130—134° (lit.,[8] b. p. 135°).

Phosphorous tri-(N-methylanilide). Phosphorus trichloride (13·75 g.) was added, with stirring and ice-cooling, to *N*-methylaniline (64·2 g.) in ether (500 ml.). After refluxing for 2 hr., the mixture was cooled and base hydrochloride removed by filtration. Evaporation of the filtrate to dryness gave a deliquescent solid which, on recrystallisation from benzene, gave *phosphorous tri-(N-methylanilide)* (30 g., 86%) as prisms, m. p. 208—209° (Found: N, 11·9. $C_{21}H_{24}N_3P$ requires N, 12·0%).

This anilide (11·4 g.), dissolved in a little anhydrous chloroform, was treated with chlorine (2·33 g.). The solution was evaporated under reduced pressure and the solid residue treated with butan-1-ol (2·5 g.); there was no reaction. Water (100 ml.) was then added and the mixture heated on a steam-bath for an hour. After cooling, the solid product was washed with 2N-hydrochloric acid and water; recrystallisation from ethanol gave phosphoric tri-(*N*-methylanilide) (10·9 g., 92%), m. p. 162° (lit.,[9] m. p. 162°).

We thank Mr. V. Manohin for the microanalyses.

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[*Received, July 1st,* 1957.]

[8] Kokatnur, *J. Amer. Chem. Soc.*, 1919, **41**, 120.
[9] Michaelis, *Annalen*, 1903, **326**, 129.

943. *Potassium Fluoromanganate*(III).

By R. D. Peacock.

Although potassium aquopentafluoromanganate(III) is sometimes prepared in the laboratory as a student exercise, the existence of the anhydrous complex fluoride K_3MnF_6 appears to have been overlooked, perhaps because it cannot be made from aqueous solution. We have prepared it by a method similar to that used to isolate potassium fluororhodate(III) and potassium fluororuthenate(III), *viz.*, the treatment of a suitable salt, in this case the complex aquofluoride, with anhydrous potassium hydrogen difluoride.

Potassium fluoromanganate(III) is a bluish-violet powder, stable indefinitely in the atmosphere at ordinary temperatures. It dissolves in dilute hydrofluoric acid re-forming the aquo-complex, but is decomposed by warm water to hydrated manganese sesquioxide Mn_2O_3,nH_2O. The magnetic moment ($\mu = 4{\cdot}95$ B.M.) indicates the four unpaired spins expected for Mn^{3+}. *X*-Ray photographs show the unit cell to be tetragonal (Table) with a large unit cell; the stronger lines can, however, be indexed on a smaller tetragonal pseudo-cell related to that of other cryolites.

In view of discrepancies in the literature regarding cryolite structures, the compounds K_3CrF_6 and K_3FeF_6 have also been made by the same technique; they then show a very slight tetragonal modification of their cubic structures reported by Bode and Voss.[2] However, small distortions of this kind have been noticed for several other cryolites at the ordinary temperature; they have been variously explained as being due to changes of composition [1] or to temperature effects causing rotation of the MF_6^{3-} octahedra about one axis.[2]

The distortion of potassium fluoromanganate(III) is obviously of a different kind, since the *c*/*a* axis ratio is reversed. Furthermore, in other cryolite structures the MF_6^{3-} octahedra can be regarded as approximately regular, but in K_3MnF_6 the distortion is so great that this is unlikely to be true. Crystal-field theory predicts [3] that a large Jahn–Teller distortion should occur for the d^4 electronic configuration attained in tervalent manganese, and this has recently been observed in manganese trifluoride [4] where two of the Mn–F bonds in each MnF_6 octahedron are considerably longer than the other four.

It is tempting to assume that in K_3MnF_6 the cell dimensions indicate the alternative distortion whereby two bonds in each MnF_6^{3-} octahedron are *shorter* than the other four. If, however, it is assumed that there are two *longer* bonds in each octahedron, it is still possible to have a unit cell with the required *c*/*a* ratio provided the cell edges are at least doubled. The available data therefore agree with either explanation.

The observed molecular volumes (Table) are important inasmuch as they suggest that in this kind of distortion the lengthening of some bonds is exactly compensated for by the shortening of others.

Experimental.—Potassium fluoromanganate(III). The aquo-salt K_2MnF_5,H_2O was prepared by Palmer's method [5] (Found: Mn, 22·0. Calc. for K_2MnF_5,H_2O: Mn, 22·3%). Potassium hydrogen difluoride was prepared from " AnalaR " reagents and dried at 100° before use.

Unit cells of potassium fluorochromate(III), *fluoromanganate*(III), *and fluoroferrate*(III) (Å).

CrF_6^{3-}	a_0 8·56, c_0 8·62, Molecular volume **631·6**
MnF_6^{3-} *	a_0 8·75, c_0 8·30, Molecular volume **635·5**
FeF_6^{3-}	a_0 8·59, c_0 8·66, Molecular volume **639·0**

* Pseudo-cell. True cell has $a_0 = 17{\cdot}50$; $c_0 = 16{\cdot}60$ A.

[1] Brosset, *Arkiv Kemi, Min., Geol.*, 1946, **21**, *A*, 142.
[2] Bode and Voss, *Z. anorg. Chem.*, 1957, **290**, 1.
[3] Orgel, *J.*, 1952, 4756.
[4] Hepworth, Jack, and Nyholm, *Nature*, 1957, **179**, 211.
[5] Palmer, " Experimental Inorganic Chemistry," Cambridge Univ. Press, 1954, p. 479.

The aquo-salt was added little by little to a large excess of molten potassium hydrogen difluoride to form a deep bluish-purple melt. After being heated at 400° for some time all the hydrogen fluoride was evolved and the melt solidified. The solid cake was allowed to cool and potassium fluoride leached out of it with formamide. The resulting *powder* was washed with acetone and ether and air-dried (Found: Mn, 18·8; F, 40·0. K_3MnF_6 requires Mn, 19·2; F, 39·8%).

Potassium fluorochromate(III) *and fluoroferrate*(III). With the aquo-salts K_3CrF_6,H_2O and K_2FeF_5,nH_2O as starting materials, the same technique as used for the fluoromanganate(III) gave the *salts* [Found: Cr, 18·7; F, 40·0. K_3CrF_6 requires Cr, 18·4; F, 40·2%. Found: Fe, 20·1; F, 39·7. K_3FeF_6 requires Fe, 19·5; F, 39·7%.]

Analysis. Manganese(III) was estimated iodometrically with thiosulphate; iron and chromium gravimetrically after precipitation of the hydroxides, and fluorine gravimetrically as lead chlorofluoride.

X-*Ray photographs.* Powder photographs were obtained on 19-cm. cameras with Co-$K\alpha$, Fe-$K\alpha$, or Cr-$K\alpha$ radiation as was most suitable. The magnetic moment of K_3MnF_6 at 25° was determined by the Gouy method.

I am indebted to Dr. J. D. Dunitz for valuable discussion of the interpretation of the experimental results.

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[*Received, July 26th*, 1957.]

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944. *The Oxidation of Hydrazine by Iron*(III) *in Acid Aqueous Solution.*

By D. R. ROSSEINSKY.

RECENT investigations of the oxidation of hydrazine by iron(III) in acid solution have led to two similar suggestions for the mechanism of reaction. The main difference is that the back reaction (−1) is omitted by Cahn and Powell [1] but is included by Higginson and Wright.[2]

$$Fe^{III} + N_2H_4 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Fe^{II} + N_2H_3 \quad \ldots\ldots\ldots \quad (1), (-1)$$

$$2N_2H_3 \xrightarrow{k_2} N_4H_6 \quad \ldots\ldots\ldots\ldots \quad (2)$$

followed by

$$N_4H_6 \longrightarrow N_2 + 2NH_3 \text{ (fast)}$$

$$2N_2H_3 \xrightarrow{k_3} N_2H_2 + N_2H_4 \quad \ldots\ldots\ldots \quad (3)$$

followed by

$$N_2H_2 - 2e \longrightarrow N_2 \text{ (fast)}$$

$$Fe^{III} + N_2H_3 \xrightarrow{k_4} N_2H_2 + Fe^{II} \quad \ldots\ldots\ldots \quad (4)$$

followed by

$$N_2H_3 - 2e \longrightarrow N_2 \text{ (fast)}$$

The values obtained for k_3/k_2 from measurements following the two mechanisms are 0·15 and <0·02 respectively. Cahn and Powell state " Although cupric ion does not react at an appreciable rate with hydrazine in acid solution, nor change the rate of oxidation of hydrazine by ferric ion, its presence greatly increases the relative amount of four-electron oxidation " [*i.e.*, by catalysis of reaction (4)]. Actually according to their mechanism a small increase, not greater than 7%, in the rate of disappearance of hydrazine would be

[1] Cahn and Powell, *J. Amer. Chem. Soc.*, 1954, **76**, 2568.
[2] Higginson and Wright, *J.*, 1955, 1551.

expected in the presence of copper(II), as reaction (3) becomes less important. If the mechanism favoured by Higginson and Wright were correct, copper(II) should increase $d[N_2H_4]/dt$ greatly by reducing the extent of the back reaction (−1). We have now measured $d[N_2H_4]/dt$ in the absence of copper(II) and with different amounts of it.

The results are shown in the Table together with (Calc.) the maximum rate (values from Expt. 1 plus 7%) expected in the presence of copper(II), if $k_{-1} = 0$. These results provide clear evidence for a large catalytic effect and hence the back reaction (−1) must be appreciable since, in similar experiments in the absence of iron(III), copper(II) alone did not oxidise hydrazine. Initial rates are similar in all experiments since the back reaction (−1) is negligible in the early stages when the concentration of iron(II) is small. (This allowed the evaluation of k_1 in these conditions as 0·48 l. mole^{-1} hr.$^{-1}$.) As the reaction proceeds and iron(II) accumulates, the difference in rates in the presence and absence of copper(II) increases in accordance with expectations based on Higginson and Wright's mechanism.

Values of the rate, $10^4 d[N_2H_4]/dt$ *(mole l.*$^{-1}$ *hr.*$^{-1}$*), at various molar concentrations of reagents.*

$[H_2SO_4] = 0{\cdot}75$M; initial $[N_2H_4] = 0{\cdot}014$M; initial $[Fe^{III}] = 0{\cdot}12$M; Temp. = 50°.

Expt.	$[CuSO_4]$	$10^3[N_2H_4]$ =	13	11	9	6	4	3·5	3·0	2·5	2·0
1	0	Rate =	41	35	21	10	5·4	4·1	3·0	2·6	1·2
2	0·025		41	35	22	12	7·2	5·8	4·3	3·7	3·2
3	0·05		41	35	22	13	8·1	7·1	5·8	4·4	3·5
4	0·075		41	35	24	14	9·1	7·5	6·0	4·8	3·7
Calc.	Maximum		—	—	22	11	5·8	4·4	3·2	2·8	1·3

Experimental.—The stock solution prepared from " AnalaR " hydrazine sulphate was standardised by Andrews's method and kept in the dark under nitrogen. Iron(III) sulphate stock solution, standardised iodometrically by titration with sodium thiosulphate, was prepared by dissolving Hilger H.P. iron in " AnalaR " sulphuric acid, followed by oxidation with inhibitor-free hydrogen peroxide, the excess of which was removed by gentle heating. 0·5M-Copper(II) sulphate and 0·5M-magnesium sulphate stock solutions were prepared from " AnalaR " reagents.

The kinetic experiments were conducted in conditions similar to those of Cahn and Powell. Magnesium sulphate was used to maintain the same total sulphate concentration, when the concentration of copper(II) sulphate was varied, by keeping $[MgSO_4] + [CuSO_4] = 0{\cdot}10$M. Higginson and Wright's procedure was followed, except that hydrazine concentrations were measured. Samples were withdrawn for analysis at the start of the experiment, and then at intervals increasing from 15 min. to 1 hr.; final readings were taken after 24 hr.

After the samples were quenched in potassium iodate solution, the iodine liberated was twice extracted with carbon tetrachloride and estimated by optical density measurements at 510 mμ on a Unicam S.P. 500 spectrophotometer. The optimum iodate concentration for the quantitative production of iodine was 0·05M, the slow reaction between iron(II) and iodate being negligible, during the short extraction period, at that concentration. Copper(II), magnesium, and iron(III) at the experimental concentrations did not affect the determination, the accuracy of which was ±4%.

Plots of hydrazine concentration against time were drawn and gradients obtained at the hydrazine concentrations quoted in the Table. These are considered to be accurate to ±8%.

The residual reaction solutions of experiments 1 and 4 were heated to 90° for 1 hr. to complete reaction, and titration of the iron(II) with potassium permanganate showed the stoicheiometries in the absence and presence of copper(II) to be 1·27 and 3·83 equiv. of oxidant per mole of hydrazine, respectively, in accord with Cahn and Powell's results.

The author thanks Dr. W. C. E. Higginson for helpful discussion, and Rhodes University for a Union Scholarship.

THE UNIVERSITY, MANCHESTER, 13. [*Received, July 4th,* 1957.]

945. *The Urea–Formaldehyde Polycondensation. Part II.* The Alkaline Hydrolysis of Alkoxymethylureas.*

By A. S. Dunn.

Using the technique described in Part I,* we have investigated the rates of alkaline hydrolysis of other alkoxymethylureas, $R{\cdot}O{\cdot}CH_2{\cdot}NH{\cdot}CO{\cdot}NH_2$. At 25° and ionic strength 1·0 the catalytic coefficients for hydroxyl ions, k_{OH^-}, are: R = Et, $1{\cdot}23 \times 10^{-4}$; R = Bu^n, $1{\cdot}22 \times 10^{-4}$; R = Bu^i, $2{\cdot}0 \times 10^{-4}$ l. mole^{-1} sec.$^{-1}$. Under the same conditions the value for methoxymethylurea * was $3{\cdot}05 \times 10^{-4}$ l. mole^{-1} sec.$^{-1}$.

For ethoxymethylurea the rate of hydrolysis at a sodium hydroxide concentration of 0·5N decreased linearly as the ionic strength was increased to 2·5; at a lower hydroxide concentration, 0·1N, this effect was much less marked. The temperature dependence of the catalytic constant is given by $k_{OH^-} = 2{\cdot}34 \times 10^9 \exp(-18{,}100/\boldsymbol{RT})$; this energy of activation is 2 kcal./mole higher than that for methoxymethylurea.*

British Rayon Research Association,
Heald Green Laboratories, Wythenshawe, Manchester, 22. [*Received, July 4th*, 1957.]

* Part I, *J.*, 1957, 1446.

946. 1-*Ethyl*-2-*methyl*-5-*nitrobenziminazole.*

By R. Foster.

Recently 1-ethyl-2-methyl-6-methylaminobenziminazole was prepared[1] by a sequence of reactions involving ethylation of 2-methyl-5(6)-nitrobenziminazole to a pair of isomers, in the proportion of 8 : 1 by weight. By analogy with Philips's work,[2] we assumed that the more abundant isomer (m. p. 142°) was 1-ethyl-2-methyl-6- and the other (m. p. 176°) was 1-ethyl-2-methyl-5-nitrobenziminazole.

1-Ethyl-2-methyl-5-nitrobenziminazole has now been synthesised unambiguously. *N*-Ethyl-2 : 4-dinitroaniline was reduced to *N*-ethyl-4-nitro-*o*-phenylenediamine by ammonium sulphide in pyridine. This with acetic acid gave 1-ethyl-2-methyl-5-nitrobenziminazole, identical with the above isomer, m. p. 176°.

Catalytic reduction of 1-ethyl-2-methyl-5-nitrobenziminazole gave the 5-amino-compound, and reduction of the formyl derivative gave the 5-methylamino-compound. The latter was prepared as a possible antagonist of 5-hydroxytryptamine.[1]

Experimental.—*1-Ethyl-2-methyl-5-nitrobenziminazole.* 1-Chloro-2 : 4-dinitrobenzene (76 g.) was added slowly to 30% w/w alcoholic ethylamine (100 ml.) and anhydrous cupric chloride (2 g.). Much heat was evolved. The mixture was cooled to room temperature and the solid removed. After repeated washing with water, *N*-ethyl-2 : 4-dinitroaniline (91%) had m. p. 113·5° (Stoermer[3] gives m. p. 114°). This was reduced without further purification, by ammonium sulphide in pyridine.[4] *N-Ethyl-4-nitro-o-phenylenediamine* was recrystallised twice from methanol, to give dark red plates (50%), m. p. 140° (Found: C, 53·3; H, 6·0; N, 23·5. $C_9H_{11}O_2N_3$ requires C, 53·0; H, 6·1; N, 23·2%). This diamine (12 g.), 4N-hydrochloric acid (180 ml.), and acetic acid (30 ml.) were refluxed for 8 hr. The product was precipitated by an

[1] Foster, Ing, and Rogers, *J.*, 1957, 1671.
[2] Philips, *J.*, 1931, 1143.
[3] Stoermer, *Ber.*, 1898, **31**, 2531.
[4] Brady, Day, and Reynolds, *J.*, 1929, 2264.

excess of ammonia and twice recrystallised from aqueous ethanol (50% v/v). 1-*Ethyl*-2-*methyl*-5-*nitrobenziminazole* was obtained as pale yellow needles, m. p. 176° (92%) alone or mixed with the higher-melting isomer mentioned above (Found: C, 58·9; H, 5·5; N, 20·7. $C_{10}H_{11}O_2N_3$ requires C, 58·5; H, 5·4; N, 20·5%). This material and the previous sample had absorption max. at 307 (ε 9500—9700) and 241 mμ (ε 25,000) in MeOH at 20°. The isomer, m. p. 142°, had max. at 310 (ε 10,100) and 240 mμ (ε 19,000) in MeOH at 20° and, mixed with the 5-nitro-compound, melted at 139—140°.

1-*Ethyl*-2-*methyl*-5-*methylaminobenziminazole*. 1-Ethyl-2-methyl-5-nitrobenziminazole was hydrogenated in alcohol over Raney nickel at 7 atm. for 1 hr. The amine (95%) did not crystallise. The *picrate* formed orange needles, decomp. *ca.* 210°, from aqueous methanol (30% v/v) (Found: C, 48·1; H, 4·4; N, 20·7. $C_{10}H_{13}N_3,C_6H_3O_7N_3$ requires C, 47·5; H, 4·0; N, 20·8%). The amine (10 g.), 98—100% formic acid (100 ml.), and toluene (200 ml.) were slowly distilled on a steam-bath. After 6 hr., when 280 ml. of liquid had distilled, the remainder was evaporated *in vacuo*, and the residual solid dissolved in the minimum of water, basified with solid sodium hydrogen carbonate, and extracted with chloroform. The solution gave, on evaporation, 1-*ethyl*-5-*formamido*-2-*methylbenziminazole* which, crystallised from ethyl methyl ketone, had m. p. 217° (yield 60%) (Found: C, 65·0; H, 6·4; N, 20·2. $C_{11}H_{13}ON_3$ requires C, 65·0; H, 6·4; N, 20·7%). The formyl compound (5 g.) was added slowly to a solution of lithium aluminium hydride (5 g.) in dry ether. Then the mixture was refluxed with vigorous stirring for 2 hr. The excess of hydride was decomposed by wet ether, and finally water. The ethereal solution was decanted and on evaporation gave 1-*ethyl*-2-*methyl*-5-*methylaminobenziminazole* which was recrystallised three times from ethyl acetate, forming prisms (60%), m. p. 134·5° (Found: C, 69·3; H, 7·7; N, 22·2. $C_{11}H_{15}N_3$ requires C, 69·8; H, 7·9; N, 22·2%).

This work was carried out during the tenure of an Edward A. Deeds Fellowship of the University of St. Andrews.

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[*Received, July 4th*, 1957.]

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